







## International Forum on the Collection and Use of COVID-19 Convalescent Plasma: Responses

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### United States – Vitalant

Mark Yazer & Darrell Triulzi

#### Question 1

Vitalant in Pittsburgh administers a centralized transfusion service that provides transfusion medicine expertise and blood products to about 24 area hospitals. Between these hospitals, virtually all medical and surgical services are provided from neonatal to geriatric care, including several Level 1 trauma hospitals. Vitalant Pittsburgh is also the regional blood collector, collecting approximately 87 000 RBCs, 25 000 platelets, and 31 000 plasma units per year.

#### Question 2

CCP is collected at Vitalant by apheresis. Our collection of CCP is the same as for routine plasma apheresis donations in that, according to the US FDA, plasma can be donated every 28 days, up to 13 times per year. While the FDA allows donors to give plasma more frequently, as soon as 48 h apart, these are considered frequent plasma donors and require close monitoring. The FDA waived the frequent donor requirements temporarily during the pandemic. The Vitalant blood donor medical director can give medical approval for donation more frequently than 28 days on a donor-by-donor basis.

#### Question 3

CCP is collected for transfusion to patients with dyspnoea and a positive COVID-19 diagnosis. Initially, we provided CCP for use in both compassionate and study protocols, in particular the Mayo Clinic study. However, since the Mayo Clinic IND was completed, all of the CCP is provided as an investigational new drug and the physician who orders it is required to explain the investigational nature of the product to the patient and document the patient's understanding of this fact in the consent note.

#### Question 4

Yes, a donor must have a positive test indicating that they were infected with COVID-19. We accept the results of either the PCR or the antibody test as proof that they were infected.

The donor must wait 28 days after resolution of their last sign or symptom before they can donate CCP.

#### Question 5

No.

#### Question 6

As a service to the community, and as a means of identifying potential CCP donors, Vitalant tests all donors who

donate whole blood or apheresis products for these antibodies. This testing is performed after the donation is made and the donor can check their results on the website. Similarly, potential donors who are referred to the blood centre by the hospital to donate CCP once they have recovered from their infection are also tested for antibodies after the donation is made. Thus, having a high titre antibody is not an exclusion criteria as the titre is determined after the donation is made.

#### Question 7

Vitalant uses the Euroimmun IgG/IgA immunoassay, with the donor plasma diluted 1:100.

Yes, samples are frozen for future assessment.

#### Question 8

No, our CCP does not undergo pathogen inactivation.

#### Question 9

No.

#### Question 10

Yes, individuals who have recovered from COVID-19 can donate standard blood products 28 days after resolution of their last sign or symptom.

#### Question 11

No.

#### Question 12

1. Substantial coordination was needed between hospitals, testing sites, in order to streamline the referral of potential donors to the blood centre.
2. Donor recruitment is still a challenge
3. Educating the ordering physicians about clinical criteria, dose, and what is required in order to obtain informed consent is a challenge given the wide range of physicians who treat COVID-19 patients. We found it best to have a small group of hospital-based clinicians who were trained in the appropriate and up-to-date use of, and consent for, CCP approve its use and ensure that the proper documentation has been obtained on each patient.

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## Turkey – Bursa Transfusion Centre

Levent Tufan Kumaş

#### Question 1

- Type of institution
  - *Hospital-based Blood Services* (a hospital unit performing the functions of blood establishment and transfusion services at a hospital level)
- Institution demographics

For hospital

- Number of in-patient beds: 900
- Approximate number of RBCs transfused/year: 22 000
- Age group of patients treated: Neonates, paediatrics <18 years, adults >18 years.
- Type of patients treated: Both medical and surgical.

For blood establishments and blood services

- Whole blood donation number: 20 000/year
- Apheresis donation number for platelets: 1700/year (3300 units of apheresis platelet concentrates prepared totally)

#### Question 2

We perform *plasmapheresis* for collection of CCP.

Donation frequency permitted for routine plasma donation by apheresis: 48 h (Max. twice a week, totally 33 donations/year).

Donation frequency permitted for CCP donation by apheresis: 10 days (Max. 8 donations in a 3 months period).

#### Question 3

CCP is collected for *transfusion*, and for compassionate use.

#### Question 4

Yes. Diagnosis of COVID-19 infection by a laboratory test result (Either PCR test positivity studied from the

nasopharynx swab sample or serologically test positivity for SARS-CoV-2 antibodies) is considered acceptable. In addition to general blood donor selection criteria: 28 days after complete cessation of COVID-19 symptoms donors considered to be acceptable for CCP donation Or, 14 days after complete cessation of COVID-19 symptoms with 2 negative PCR test results (One of the tests must have been done within the last 48 h).

#### Question 5

No.

#### Question 6

Yes. SARS-CoV-2 IgG assay (Abbott Architect). Chemiluminescent microparticle immunoassay. Predefined index value threshold of 1.4 signal-to-cut-off (S/C) ratio for seropositivity. (Tests are run just before each donation process).

#### Question 7

No. The samples are collected from the CCP unit and freezed/archived for future assessment.

#### Question 8

No.

#### Question 9

No.

#### Question 10

Yes. The minimum deferral period after recovery before whole blood or apheresis donation is 28 days.

#### Question 11

No. According to our regulations; these people are considered to be people who have received a blood transfusion, so they cannot donate blood or plasma at least 12 months.

#### Question 12

- In the first step, we had difficulties in supplying an antibody test that meets the national guideline requirements to be used in our institution to select available donors for CCP apheresis.

- At the beginning of the pandemic (April to June), the donor organization and the referral of suitable donors to our blood centre was done by the local health authority. However, as this organization is not maintained and there are not enough volunteer donors at the moment, most of our CCP donors are replacement donors.
- High donor deferral rate (General blood donor selection criteria, negative anti-SARS-CoV-2 antibody test results, and deferral of female donors due to pregnancy history) and short donation period (Max. 3 months) make it difficult to prepare sufficient number of products.
- Another challenge is not measuring the neutralizing antibody titre in the prepared products before transfusion.

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## Turkey – Turkish Red Crescent

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#### Question 1

- Type of institution
- **National Blood Services/Blood Centre** (responsible for recruiting donors; screening and selecting blood donors; blood collection; testing and processing blood units; transporting; receiving and storage of blood units; pre-transfusion testing, and issuing blood for clinical transfusion at a national level)
- Institution demographics
  - Year 2019:
    - Blood Donation Number: 2-766-581
    - Apheresis Donation Number: 42-656
    - RBC production: 2-738-117
    - Fresh Frozen Plasma (FFP) Production: 1-390-223
    - Pooled platelet production: 281-327
    - Apheresis Platelet Production: 44-726
  - Year 2020 (11 month):
    - Blood Donation Number: 2-126-279
    - Apheresis Donation Number: 55-247
    - Convalescent Plasma (CP): 35-383
    - RBC production: 2-110-140
    - Fresh Frozen Plasma (FFP) Production: 1-098-723
    - Pooled platelet production: 244-554
    - Apheresis Platelet Production: 77-429
    - Apheresis CP Production: 63-145

**Question 2**

- *Immune plasma donation can be done within a minimum of 14 days and a maximum of 3 (three) months after recovery. The date of the first donation is accepted as the starting date and it can be made 8 times in 3 months with a minimum of 10 days intervals and a maximum of 3 times in a month. A maximum of 1800 ml of plasma can be collected from a donor in one month.*
- *No*

**Question 3**

- *Turkish Red Crescent is responsible for procurement. Indications for use should be taken from the Ministry of Health or from faults.*

**Question 4**

- *In order for individuals caught and recovered from COVID-19 virus infection to become donors:*
  - *The diagnosis of COVID-19 infection was made according to the results of the laboratory test (PCR test positivity from the nasopharynx swab sample or the test positivity of SARS-CoV-2 antibodies serologically) AND*
  - *At least 14 days have passed since clinical recovery (cough, fever, shortness of breath, weakness, etc.) AND*
  - *At least 2 PCR test results from nasopharyngeal swab samples must be negative (one of the tests must have been done in the last 48 h).*
  - *If 28 days have passed since clinical recovery, PCR test negativity is not required. The records of these people should be complete, documented and traceable.*

**Question 5**

No

**Question 6**

No

**Question 7**

Yes. ELISA (17 Regional Blood Center) and CLIA (1 regional blood center) (Euroimmun/Roche)

If yes/no, are samples collected from the CCP unit and freeze/archived for future assessment? YES

**Question 8**

Yes. Mirasol® Pathogen Reduction Technology - Terumo BCT

**Question 9**

No. These people are considered to be people who have received a blood transfusion, so they cannot donate blood or plasma

**Question 10**

Yes. 28 days.

**Question 11**

No. These people are considered to be people who have received a blood transfusion, so they cannot donate blood or plasma.

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**Turkey – Acibadem Health Group Hospitals**

Nil Banu Pelit

**Question 1**

- Type of institution
- **Hospital-based blood transfusion service/blood bank** (a hospital unit responsible for pre-transfusion and compatibility testing, and issuing blood for clinical transfusion exclusively for use within hospital facilities)
- Institution demographics
  - For hospital
    - Number of in-patient beds: 2129/16 hospitals
    - Approximate number of RBCs transfused/year: 44 465 between Nov 2019–2020
    - Age group of patients treated (neonates, paediatrics <18 years, adults >18 years): <18 y: 19 500 >18 y: 72 000
    - Type of patients treated (medical or surgical): M:68500; S: 23000
  - For blood establishments and blood services
    - Approximate number of whole blood and apheresis collections made/year for RBCs, platelets and plasma (as applicable): WB: 1080; Aph: 5800

**Question 2**

Immune plasma donation can be done within a minimum of 28 days and a maximum of 3 (three) months after recovery. The date of the first donation is accepted as the starting date and it can be made eight times in 3 months with a minimum of 10 days intervals and a maximum of three times in a month.

**Question 3**

Both.

**Question 4**

The diagnosis of COVID-19 infection was made according to the results of the laboratory test (PCR test positivity from the nasopharynx swab sample or the test positivity of SARS-CoV-2 antibodies serologically) AND.

At least 28 days have passed since clinical recovery (cough, fever, shortness of breath, weakness, etc.) AND.

At least 2 PCR test results from nasopharyngeal swab samples must be negative (one of the tests must have been done just before donation) AND.

The result of Anti-SARS-Cov-2 antibodies is IgG Positive but IgM Negative.

If there is no symptoms (weakness, cough, shortness of breath, etc.), he/she is accepted for donation.

**Question 5**

Yes, patients with negative nasopharyngeal swab test were accepted as a suitable donor.

**Question 6**

Yes, the donors are screened with rapid card tests for anti-SARS-CoV-2 IgG and IgM in donor serum/plasma. The donors who are IgG positive and IgM negative were accepted as donors.

**Question 7**

No.  
Yes.

**Question 8**

Yes: Cerus Corporation, Intercept Blood System.

**Question 9**

No. According to our regulations, these people are considered to be people who have received a blood

transfusion, so they cannot donate blood or plasma at least 12 months.

**Question 10**

Yes, at least 28 days have passed since clinical recovery (cough, fever, shortness of breath, weakness, etc.)

**Question 11**

No. According to our regulations, these people are considered to be people who have received a blood transfusion, so they cannot donate blood or plasma at least 12 months.

**Question 12**

We had developed a project for CCP collection soon after first case in Turkey was defined. In addition to the described criteria, we also prepared cryopoor plasma and pooled plasma from them in order to decrease the coagulation factors and the effect of antibody-dependent enhancement of infection. We screened the isohemagglutinin titres before pooling. We pooled 8 units in order to have the titres below 1:32. We divided this pooled plasma into 200 ml bags. By this way, we made a composition that can be used by each patient without blood group match. We will soon publish the results of this project. At the beginning of the pandemic the CCP was used in ICU patients who had pneumonia according the MoH guidelines, however the guideline was reviewed and CCP was advised during the first 7–10 days of the infection. We think that immune plasma is more useful at initial days in order to prevent the development of pneumonia or in patients in risk groups such as medical staff and close contacts to infected people.

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**Canada – Héma-Québec**

Renée Bazin

**Question 1**

- Type of institution
  - Héma-Québec is the National blood establishment for the Province of Quebec, Canada
- Institution demographics
  - For blood establishments and blood services
    - Approximate number of whole blood donations/year: 220 000

- Approximate number of RBC apheresis collections/year: 2000
- Approximate number of platelet apheresis collections/year: 40 000
- Approximate number of plasma apheresis (750 ml) collections/year: 25 000
- Approximate number of plasma (250 ml) apheresis collections (multiple components)/year: 2500

#### Question 2

- CCP donation is done by plasmapheresis only at our institution. We collected CCP between April and July 2020 and will resume collection in January 2021. Donors are allowed to donate every 6 days, in accordance with our standard procedures for regular plasma donations. Between April and July, donors were allowed to donate for up to 12 weeks after their first donation. Starting in January 2021, donors will be allowed to donate for a maximum 6 weeks after resolution of their symptoms. This change is introduced to reflect the waning of antibodies to SARS-CoV-2 (both total and neutralizing antibodies) occurring rapidly after symptom onset. We observed this decline during the characterization of CCP collected from repeat donors at our institution and reported it in several scientific publications [1-3].

#### Question 3

- CCP collected between April and July 2020 is used exclusively in one of the three clinical trials for the treatment of COVID-19 patients currently underway in Canada. Plasma collected from January 2021 will also be dedicated to clinical trials but with the possibility of redirecting units not qualified for clinical trials to other uses such as fractionation or research projects, provided that donors have consented to these potential uses.

#### Question 4

- Recovered COVID-19 patients are recruited for CCP donation mostly following self-identification and through social media. All participants must have received a diagnosis of COVID-19 by the Québec Provincial Health Authority through either PCR or epidemiologic contact. They also have to meet the donor selection criteria for plasma donation in use at our institution. They are allowed to donate plasma at least 14 days after complete resolution of COVID-19

symptoms (fever, cough), which is the same criterion applied for recovered COVID-19 patients who choose to donate regular blood donations instead of CCP.

- Males and females with no history of pregnancy meeting the above criteria are invited to donate CCP after informed consent.

#### Question 5

- No test to confirm clearance of the infection is required before donation at our institution. The same rule applies to regular blood donations, in compliance with Health Canada regulations.

#### Question 6

- Donors are not tested for the presence of anti-SARS-CoV-2 in their plasma prior to donation. Plasma is collected from recovered individuals who meet the criteria for CCP donation and then tested for the presence of anti-SARS-CoV-2 antibodies within one week of donation using an in-house RBD ELISA test.

#### Question 7

- All CCP units are tested at our institution using an in-house SARS-CoV-2 RBD ELISA. Seropositivity is defined as an ELISA result above the cut-off value at a 1:100 plasma dilution [1]. This value was calculated using the mean OD + 3 SD of COVID-negative plasma samples (collected before the outbreak of SARS-CoV-2) plus a 15% inter-assay coefficient of variation. Additional tests to further characterize CCP are performed at our external collaborators' laboratories (total spike antibodies, neutralization and ADCC assays).
- Retention samples for all CCP are kept in case of need for future assessment.

#### Question 8

- CCP is not subjected to a pathogen reduction treatment at our institution.

#### Question 9

- At our institution, all plasma recipients are deferred from donating blood products for a period of 6 months. The same criterion is applicable to CCP recipients. As a result, these individuals will not be accepted for CCP donations after the deferral period because of the long delay after symptom resolution, which exceeds the 6 weeks donation period set for CCP donations.

**Question 10**

- Our institution accepts individuals recovered from COVID-19 infection for standard whole blood or apheresis donations, after a minimum deferral period of 13 days after recovery. In other words, donors are accepted 14 days after complete resolution of their COVID-19 symptoms.

**Question 11**

- As for all other recipients of blood products, recipients of CCP are deferred from donating blood products for a period of 6 months after which period they are welcomed to donate blood products.

**Question 12**

- When setting up the CCP collection program at our institution, we faced many challenges such as the need to rapidly recruit donors, collect and test CCP while maintaining adequate inventories of other blood products, especially those collected using the same equipment (competition for apheresis machines). Other challenges included the frequent changes in regulatory requirements regarding donor eligibility during program initiation, which led to several adjustments in a short time. In addition, the need to rapidly develop and validate an anti-SARS-CoV-2 assay given the uncertainty over the short-term availability of commercial assays in April 2020. One of the most important lessons learned is that the rapid implementation of a new activity such as CCP program requires coordinated efforts from every service (particularly Operations, QA, Regulatory affairs, IT and Medical Affairs) as well as a clear and collective understanding of the objectives underlying the project. Establishing a CCP collection program in our institution turned out to be a very motivating endeavour for all participants, allowing them to make a difference in the efforts to fight COVID-19.

**Section References**

- 1 Perreault J, Tremblay T, Fournier M-J, et al. Waning of SARS-CoV-2 RBD antibodies in longitudinal convalescent plasma samples within four months after symptom onset. *Blood* 2020;136:2588–91.
- 2 Beaudoin-Bussièrès G, Laumaea A, Anand SP, et al. Decline of humoral responses against SARS-CoV-2 spike in convalescent individuals. *MBio* 2020;11:e02590-20.
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responses against SARS-CoV-2 spike. *Cell Reports Med* 2020;1:100126.

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**Saudi Arabia**

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**Question 1**

- Hospital-based blood services
- Institution demographics:
  - Number of in-patient beds: 780 beds
  - Approximate number of RBCs transfused/year: 12 000
  - Age group of patients treated (neonates, paediatrics < 18 years, adults > 18 years) All age groups
  - Type of patients treated (medical or surgical): Medical and surgical for all age groups but without transplant or trauma.
  - Approximate number of whole blood and apheresis collections made/year for whole blood: 12 500, which processed to blood components, apheresis platelets donation around 100

**Question 2**

Type of CCP donations in our institution is performed through plasmapheresis and donor can donate once or twice one week apart.

**Question 3**

Collected CCP is intended for transfusion of COVID-19 patients only under clinical trial and only few have been used as compassionate use.

**Question 4**

The CCP donor eligibility criteria used in our institution are as follow:

Donor should match routine donor eligibility criteria; donors should have history of SARS-CoV-2 infection with positive confirmation for SARS-CoV-2 by PCR testing and complete recovery from symptoms of at least 2 weeks before donation.

There is no need to have a confirmatory test result status of past COVID-19 infection before CCP donation but anti-SARS-CoV-2 neutralizing antibodies titre regularly done for all donors at time of donation.

#### *Question 5*

No need to test the CCP donor for SARS-CoV-2 by PCR before donation as he should have complete clinical recovery for 2 weeks before CCP donation.

#### *Question 6*

To date, we are testing all donors for SARS-CoV-2 neutralizing antibodies titre before donation through in-house neutralization test using live virus. No other antibody testing is done.

#### *Question 7*

We are testing only donors at time of CCP donation for SARS-CoV-2 neutralizing antibody titre testing.

#### *Question 8*

At our institution, CCP subjected to a pathogen reduction treatment and we use Intercept system (Amotosalen and UV light treatment).

#### *Question 9*

At the current time, the protocol does not clearly exclude recipients of CCP from CCP donation. However, we did not have come across any recipients of CCP whom like to donate. At our institution recipients of blood or blood components are deferred from donating any blood components for 3 months (new policy).

#### *Question 10*

Individuals recovered from COVID-19 infection can donate if 28 days have passed since resolution of symptoms, or 28 days after the date of the positive swab if they were asymptomatic.

#### *Question 11*

Recipients of blood or blood components (including recipient of CCP) are deferred from donating any blood components for 3 months. This change from the previous policy of deferral for 12 months was based on FDA guidance <https://www.fda.gov/media/92490/download>

#### *Question 12*

We faced few challenges as convincing recovered patients to donate CCP after their discharged from the hospital, as they seem to be worried about their health and contracting infection again. The other challenges are the transfusion protocol, dosing and frequency of treatment.

An important lesson we learned that the recruitment of CCP donors should be started shortly after diagnosis by healthcare professionals in contact with the patient at that early stage and before discharge from the hospital. Awareness and education to the patients and society on the importance of CCP donation and its implication through distribution of educational materials and discussion with patients, through donor campaigns and social media are essential. We should be prepared with effective plan for future pandemics if any.

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### **India – New Delhi**

Gopal K Patidar, Hem Chandra Pandey & Rahul Chaurasia

#### *Question 1*

We are a hospital-based blood transfusion service within All India Institute of Medical Sciences (AIIMS), New Delhi, India, that is one of the largest tertiary care academic hospital in North India. Our hospital has more than 2000 in-patient's hospital beds, catering to patients of all age groups i.e. neonates, paediatrics, adults and geriatrics, across all medical and surgical specialties. We received approximately 1 50 000 blood component transfusion requests form annually from various departments out of them around 75 000 red blood cell units issued annually for transfusion. At our institution, there are three blood centres under the purview of Department of Transfusion Medicine, which collects more than 80 000 of whole blood units annually and fully process it into blood components like red blood cells, platelet concentrates and plasma. We also perform pre-transfusion testing and issue the blood components within our hospital and outsource excess plasma for fractionation. We also have apheresis facilities which mainly focuses on platelet (apheresis)



collection and peripheral blood stem collection accounting for collection of 2000 apheresis units. Therapeutic procedures such as plasma exchanges are also quite frequent (400–500 plasma exchanges are performed annually). Apheresis plasma collection was not performed routinely in the pre-COVID-19 period.

### Question 2

At our institution CCP donation is done by plasmapheresis, as per the regulations mandated under the Drugs and Cosmetic Act (second amendment) 2020, India [1]. The act recommends “The quantity of plasma separated from the blood of donor shall not exceed 500 ml per sitting and once in a fortnight or shall not exceed 1000 ml per month”. Thus, allowing a CCP donor to donate twice a month with maximum collection of 500 ml in each donation.

### Question 3

At our institute, CCP collected is intended for transfusions only. During the initial phases of COVID-19 pandemic, CCP transfusions were performed as a part of clinical trial to evaluate its safety and efficacy. Later on, its use was restricted for off label indication or transfused on compassionate grounds.

### Question 4

CCP donor eligibility criteria at our institution were in accordance with national guidelines issued by Indian Council of Medical Research (ICMR) [2] and National Blood Transfusion Council (NBTC) [3], India.

Our donor eligibility criteria are as following:

1. Donor age should be 18–60 years.
2. Males or nulliparous female donors of weight >50 Kg.
3. Laboratory confirmed COVID-19 either by RT-PCR OR Rapid antigen test.
4. Recovered patient (CCP donor) preferably symptomatic during illness (fever, cold, cough, etc.) and demonstrable anti-SARS-CoV-2 IgG antibodies by available immunoassay.
5. Complete resolution of symptoms at least 14 days prior to donation, RT-PCR negative report is not mandated in this situation. If RT-PCR negative report is available, then the period can be reduced to 14 days from the negative RT-PCR report.
6. Asymptomatic donors may be accepted, if anti-SARS-CoV-2 IgG antibodies are present and verified by two different approved test.
7. In addition, donor eligibility criteria for whole blood donation is being followed in accordance with Drugs and Cosmetics (Second Amendment) Rules, 2020 [1].

8. Complete blood count including Haemoglobin (Hb), Haematocrit (HCT), Platelet count, Total leucocyte count (TLC) and differential leucocyte count (DLC). Donors with Hb > 12.5 g/dl, platelet count >1 50 000 per microlitre of blood and TLC within normal limits are accepted.
9. Donors negative for screening test of human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV), syphilis and malaria are accepted.
10. Donors with total serum protein >6 gm/dl are accepted.
11. Titration of anti-SARS-CoV-2 neutralizing antibodies may be done depending on availability of facilities at the time of testing. Unavailability of antibody titres is not preclude convalescent plasma transfusion. Desired titres for IgG antibodies is 1:640 by enzyme-linked immunosorbent assay (ELISA) method OR 13 arbitrary unit (AU) by chemiluminescence method OR for neutralizing antibodies titre of 1:80 (Plaque reduction neutralization test (PRNT)/microneutralization test (MNT).
12. Blood group (ABO grouping and Rh phenotyping) and antibody screening for clinically significant antibodies (Extended Rh, Kell, Duffy, Kidd, MNS) – Antibody screen positive donors are deferred.

### Question 5

At our institution CCP donors are not tested for SARS-CoV-2 by PCR method to confirm clearance of the infection before donation.

### Question 6

Yes, we do test the CCP donors for presence of IgG anti-SARS-CoV-2 antibodies using chemiluminescence assay in Abbott platform (i1000SR) before donation. We were using all the CCP above the cut-off recommended by the manufacturer (1.4) for differentiating positive and negative samples.

### Question 7

Pre-donation testing of blood donors for presence of IgG anti-SARS-CoV-2 antibodies is being done and repeat testing of the collected units is not done. The unit is collected either on the same day of testing or the next day. As we did not have facility for testing neutralizing titre, we do store the frozen sample of CCP for testing in future.

### Question 8

Pathogen reduction treatment for plasma is still not in use in our country, so collected CCP units were not subjected to pathogen reduction treatment.

**Question 9**

As per the regulations laid out in the Drug and Cosmetic Act (Second Amendment), 2020 [1], any blood and blood component recipient should be deferred for any donation until 12 months. Accordingly, we also do not accept recipients of CCP for convalescent plasma donation.

**Question 10**

At our institution, we accept whole blood or apheresis donation after 28 days of complete recovery after COVID-19 infection as per the guidelines issued by the National Blood Transfusion Council, India [3].

**Question 11**

As per the regulations laid out in the Drug and Cosmetic Act (Second Amendment), 2020 [1], any blood and blood component recipient should be deferred for any donation until 12 months. Accordingly, we also do not accept recipients of CCP for whole blood and apheresis donation until 12 months after receipt of transfusion.

**Question 12**

Blood collection by apheresis is not a routine procedure in our country and is limited to only platelet collections at most of the blood centres. Thus, general public in our country is less aware and motivated towards blood component donations through apheresis procedure. Motivating individuals who have recently recovered from severe mental stress due to COVID-19 for apheresis donation was a daunting task. This was subdued by continuous motivation of potential donors, especially by treating clinicians during treatment or recovery and follow-up by the blood centre staff.

Since recruiting donors for CCP donation was difficult amid the national lockdown, we had to modify our approach towards recruitment and screening of the blood donors. A telephonic screening of potential donors by asking the health related questions or sending questionnaire by digital means, allowed only the eligible donors to come at the blood centre. This not only reduced the hardships faced by the donors during travel restrictions but also helped in maintaining social distance. At times, incentivizing the donor in the form of transportation through hospital/medical vehicle, also aided them to come and donate CCP.

Since plasma donation was new procedure for most donors, the total time taken for CCP donation, including waiting time required for testing and due to the limited

apheresis equipment was also a demotivating factor for many donors. This was improved by allotting time slots for sample collection and procedure to donors and demarcating dedicated space and equipment for CCP donation.

Apart from donor-related issues, we also faced issues related to the availability of quality antibody assays to screen donors for presence of SARS-CoV-2 antibodies. The availability of neutralizing assays remains a challenge.

However, stringent CCP donor selection criterion remained a major hurdle in the overall process as it reduced the number of eligible donors significantly. A careful analysis of risk vs. benefit of certain less innocuous conditions in the donors and relaxing them, during the pandemic situation can further improve the overall recruitment of donors for CCP.

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**Brazil**

Roberta Maria Fachini, Patrícia Scuracchio & Silvano Wendel

### Question 1

- Type of institution: Hospital-based blood service
- Institution demographics:

The Hospital Sírio-Libanês is a not for profit private hospital with 510 in-patient beds that transfuses an average of 6000 red blood cells (RBCs)/year. The hospital receives paediatric and adult patients affected by clinical or surgical diseases. It is a national reference institution for oncological and critical patients, including those that need to be submitted to bone marrow transplantation, solid organ transplants, cardiovascular, orthopaedic, neurological and extensive oncological surgeries.

The Hospital Sírio-Libanês Blood Bank collects approximately 5500 whole blood units and 1750 apheresis, rendering additional 2300 components per year.

### Question 2

As no specific single therapeutic measure has been proven efficient for COVID-19 treatment yet, the transfusion of SARS-CoV-2 convalescent plasma (CCP) has been studied through clinical trials.

Only male candidates, who had a moderate/mild disease, and full clinical recovery at least for  $\geq 14$  days, with a previous positive RT-PCR, age ranging from 18 to 60 years and body weight  $> 55$  kg were accepted as potential CCP donors, according to national guidelines [1,2]. Those approved by a medical interview, were submitted to a second RT-PCR (whose result had to be negative), and had their neutralizing antibodies (nAb) tested by a virus neutralization test (VNT), and anti-nucleocapsid (NP) SARS-CoV-2 IgM, IgG and IgA ELISAs, as described elsewhere [3]. CCP units were collected only via plasmapheresis with a standard 600 mL plasma collection. According to Brazilian guidelines, each apheresis donor is allowed to donate plasma up to four times by apheresis in a two-month period; however, in specific situations, they can donate in shorter period in order to supply the transfusion demand for special patients, as COVID-19 [2].

### Question 3

All the collected CCP is intended for transfusion, mostly for clinical trials, and in lesser amount as compassionate use, depending on the medical request. For clinical trial use, admitted patients were confirmed by RT-PCR, being  $\geq 18$  years old, and with criteria for severe pneumonia (defined by respiratory distress: oxygen saturation of 93% or less on room air, respiratory rate  $> 30$  breaths/min and/or arterial partial pressure of oxygen ( $\text{PaO}_2$ )/fraction of inspired oxygen ( $\text{FiO}_2$ ) of 300 or less). Patients with

preexisting history of anaphylactic transfusion reaction, pregnant or lactating women were excluded from trials [4]. No CCP units were intended as prophylaxis or fractionation use at this moment.

### Question 4

Donors had to present a previous positive molecular test (SARS-CoV-2 RT-PCR) collected by nasopharyngeal swab at the time of the diagnosis, and full clinical recovery for at least 14 days after the beginning of their symptoms.

### Question 5

Donors approved by the medical examination underwent a second molecular test (SARS-CoV-2 RT-PCR by nasopharyngeal swab), which had to be non-reactive in order to be accepted for donation. Donors who remain reactive by the RT-PCR were invited to perform a third RT-PCR test after additional 14 days. If the subsequent RT-PCR test is non-reactive, the donor was accepted; otherwise, rejected from the CCP collection program [3]. Additionally, donors were tested for blood typing (ABO and RhD), irregular antibodies to red blood cell antigens (immunohematologic tests), and infectious diseases markers (hepatitis B and C virus, human immunodeficiency virus, human T-lymphotropic virus-1/2, syphilis and Chagas disease).

### Question 6

Serum samples were collected for a cytopathic effect (CPE)-based virus neutralization test (VNT) carried out with SARS-CoV-2 (Gen-Bank: MT MT350282) and for immunoglobulins (IgA, IgM and IgG) nucleocapsid protein (NP)-based SARS-CoV-2 enzyme-linked immune-sorbent assays (ELISA) [3] at the moment of the first medical interview, together with the second RT-PCR. Only donors with nAb titre  $\geq 160$  and a negative RT-PCR were later accepted for donation, regardless of anti-NP results.

### Question 7

Likewise, the same tests for anti-SARS-CoV-2 antibodies (nAbs and immunoglobulins) were carried out on donated CCP units, using the same criteria described above.

### Question 8

All CCP units were treated with INTERCEPT<sup>®</sup> (Cerus Corporation, Concord, USA), according to manufacturer's instructions, either individually or pooled two by two.

After treatment, units are separated into 200 ml doses. Pre- and post-treatment samples were tested for nAb titres and specific anti-NP antibodies, with no considerable change both in nAb or anti-NP levels before or after pathogen reduction [5].

#### Question 9

The answer is no, based on our current protocol, which establishes that only individuals who had mild/moderate SARS-CoV-2 infections can be candidate for donations. In addition, the Brazilian legislation [2], defines that anyone who has received a transfusion of any blood component, could donate blood only after a minimum period of 1 year.

#### Question 10

Yes, we accept individuals recovered from COVID-19 infection for standard whole blood or apheresis donation, as long as they have had the mild form of the disease and only after 60 days of complete recovery of all symptoms.

#### Question 11

See question 9.

#### Question 12

The implementation of a CCP collection program in our blood service was a very important action in order to provide specific immunological support therapy during the pandemic and to analyse the strengths and weaknesses of this program.

One of the main concerns observed was the long persistence of RT-PCR positive for more than 28-day period in 30% of the CCP donors [3], which led us to decide extending the current 28-day to 60-day period for temporarily donor rejection after being infected by SARS-CoV-2. We have also observed that specific IgG antibodies might correlate with high nAb titres as well as an interesting direct relation between body mass index (BMI) and donor nAb titres, suggesting that overweight or obese donors have more capacity to produce higher nAb levels [6].

Another issue to be highlighted was the pathogen reduction treatment (PRT) in all CCP units, whose method was already implemented in our service. To date, PRT is not a national routine in Brazil, although considered an important method for coronavirus inactivation in blood components.

The main challenge is still to define which patients would certainly benefit from this kind of therapy, since large RCT are quite difficult to be implemented in the country at this moment, despite the high number of COVID cases.

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#### Singapore

Ai Leen Ang & Kiat Hoe Ong

### Question 1

Singapore's COVID-19 Convalescent Plasma (CCP) Programme was jointly developed by the National Centre for Infectious Diseases (NCID), Tan Tock Seng Hospital (TTSH) and Health Sciences Authority (HSA). HSA is a National Blood Establishment and TTSH is a tertiary hospital that operates a hospital-based blood transfusion and therapeutic apheresis service.

While TTSH is not usually involved in blood collection, it has been specifically licensed to collect CCP for Singapore due to logistical reasons as it has close affiliations with NCID (Singapore's main referral centre for COVID-19). TTSH is responsible for the selection of suitable CCP donors referred by NCID and the collection, storage and distribution of CCP in Singapore. HSA is responsible for establishing the general blood donation criteria (non-specific for CCP but still need to be fulfilled by CCP donors), freezing and standard donation testing (non-specific for CCP) of the CCP collected by TTSH.

- Institution demographics
  - For hospital (TTSH)
    - Number of in-patient beds: >1700 beds
    - Approximate number of RBCs transfused/year: About 15 000 units/year
    - Age group of patients treated: Adults of >18 years old.
    - Type of patients treated: Medical and surgical
  - For blood establishments and blood services (HSA)
    - Approximate number of whole blood and apheresis collections made/year for RBCs, platelets and plasma (as applicable): About 117 000 whole blood collections and about 8000 apheresis collections (majority for platelets) per year.

### Question 2

TTSH collects CCP by plasmapheresis. The donation frequency for CCP was initially aligned to that of routine plasma donation by apheresis at HSA, which was a maximum of 13 donations per year with at least 4-weeks interval between donations. To allow more frequent CCP collections from donors with high SARS-CoV-2 neutralizing antibody titre, the minimum inter-donation interval was subsequently changed to 2 weeks, provided that the donors' serum albumin and globulin levels before each donation were in the reference range. Despite these changes, most CCP donors were only eligible to donate once or at most twice, mostly due to decreasing

neutralizing antibody titres. Only one donor had antibody titres high enough to donate thrice.

HSA has also established a process to convert suitable standard whole blood-derived plasma to CCP. This is meant to supplement the bulk of the CCP collected by plasmapheresis at TTSH. Male blood donors who have made standard whole blood donations will have their blood samples tested for SARS-CoV-2 neutralizing antibody titre if they declare a history of COVID-19 infection within the past 6 months. If their neutralizing antibody titres meet the minimum target, HSA will label their whole blood-derived plasma as CCP. The red cells and platelets from their whole blood donation will still be used for routine transfusion since they are accepted as standard whole blood donors for their donations. So far, there had not been any whole blood-derived plasma suitable for conversion to CCP as the neutralizing antibody titres tested were below the target level. These plasma units were labelled as standard frozen plasma and stored for routine transfusion.

### Question 3

The CCP collected in Singapore is only for therapeutic transfusion as part of a monitored expanded access programme. It is not sent for fractionation.

### Question 4

Besides the standard blood donation criteria, other donation criteria specific for CCP are:

1. History of laboratory confirmed COVID-19 infection.
  - All diagnoses of COVID-19 infections in Singapore are confirmed by laboratory tests ordered by the clinics or hospitals. This is most commonly performed by SARS-CoV-2 PCR on nasopharyngeal swabs.
  - The above test results are accessible to the NCID team who refer potential CCP donors to TTSH. The team at TTSH would also have access to the relevant COVID-19 diagnostic test results.
2. At least 28 days after clinical recovery from COVID-19.
  - The definition of clinical recovery is aligned to prevailing definition of the Ministry of Health (MOH).
  - Initially, clinical recovery was defined by resolution of fever and all clinical symptoms for at least 24 h and negative SARS-CoV-2 PCR from 2 separate nasopharyngeal swabs taken 24 h apart. This was consistent with the initial criteria for persons with history of COVID-19 infections to be de-isolated in Singapore.

- Subsequently this is changed to a time-based discharge criteria. Since end May 2020, non-immunocompromised persons with history of COVID-19 infections can be de-isolated 21 days after onset of illness without further nasopharyngeal swab PCR, if they are well. Our definition for clinical recovery was also changed accordingly to the time when they could be de-isolated without the need for negative nasopharyngeal swab PCR.
3. SARS-CoV-2 surrogate neutralizing antibody titre of at least 40. This was subsequently increased to at least 80 in early May 2020 when there were more potential CCP donors.

(Initially as a precaution, the donor's blood sample needs to be negative for SARS-CoV-2 PCR before CCP is collected from them. There were plans to remove this requirement but no further CCP donors were screened when the number of eligible donors decreased dramatically since Sep 2020 due to the low number of new COVID-19 infections in Singapore. This requirement will be removed should there be subsequent screening of new CCP donors.)

#### *Question 5*

We currently do not test the CCP donor for SARS-CoV-2 by PCR before donation to confirm clearance of the infection.

#### *Question 6*

CCP donors would be tested for SARS-CoV-2 neutralizing antibody titre to ensure that they meet the minimum antibody titre before they are accepted for CCP donation by plasmapheresis at TTSH. The titre is performed by a lab at an academic institution (DUKE-NUS Medical School) which has developed the SARS-CoV-2 surrogate virus neutralization test (sVNT) based on antibody-mediated blockage of ACE2-spike protein-protein interaction [1]. The minimum surrogate neutralizing antibody titre was initially set as 40, but this was subsequently increased to 80 in early May 2020 when there were more potential CCP donors.

#### *Question 7*

At the time of CCP donation by plasmapheresis at TTSH, the donors' blood samples are sent for SARS-CoV-2 neutralizing antibody titre again using the same method by the same lab stated in response to question 6. The CCP units collected would still be stored for future use even if the neutralizing antibody has fallen below the minimum titre of 80 at the time of donation. However, CCP units

with higher titres of 80 and above would be prioritized for use. Samples from the CCP donation are archived for future assessment.

For the conversion of suitable standard whole blood-derived plasma to CCP (see response to question 2 for details), the neutralizing antibody titre for SARS-CoV-2 is also determined using the same method by the same lab as stated in response to question 6. The minimum neutralizing antibody titre is 40 for the whole blood-derived plasma to qualify for conversion to CCP. As a routine practice, all of HSA's standard blood donations would have an archived sample kept for up to 12 months post-donation.

#### *Question 8*

The CCP in Singapore is not pathogen reduced. Pathogen reduction technology is currently also not applied to the standard plasma in Singapore.

#### *Question 9*

Those who have received any type of blood transfusion (including CCP) would need to wait for 12 months before they can make any blood donation (including CCP). This is aligned to the standard blood donation criteria. Therefore, most patients would likely not qualify as CCP donor if they have received CCP since they would need to be deferred for 12 months after their CCP transfusion, by which time their neutralizing antibody titres will likely fall too low for them to be CCP donors.

#### *Question 10*

HSA accepts individuals who have recovered from COVID-19 infection for standard whole blood or apheresis donation, at least 28 days from clinical recovery. The definition of clinical recovery is the same as that for CCP donors (please see response to question 4 for details).

#### *Question 11*

HSA accepts recipients of CCP for standard whole blood or apheresis donation at least 12 months from their CCP transfusion. This is aligned to the standard blood donation criteria, which require a deferral of 12 months from any type of blood transfusion, including CCP.

#### *Question 12*

The collection of CCP by TTSH, which is closely affiliated with the main referral centre for COVID-19 in Singapore (NCID), helps to overcome several logistical challenges,

such as identifying and recruiting suitable CCP donors. Close collaboration was needed between TTSH and HSA to establish the necessary processes and protocols to facilitate the relevant approvals for TTSH to start CCP collection in a timely manner, when the number of infections was rising in Singapore.

One challenge is in finding donors who meet the target SARS-CoV-2 neutralizing antibody titre. Only about 21% of the donors screened had SARS-CoV-2 neutralizing antibody titre of at least 80. This could be due to the mild infection in these donors who are mostly young and healthy. Prior to revising to a time-based discharge criterion for infected persons, it might also be due to the longer interval from their infection when they could be screened for CCP donation, as they initially need to meet the more stringent de-isolation criteria of two negative nasopharyngeal swab PCRs. This might have contributed to a lower neutralizing antibody titre in some of the potential CCP donors. In the later part of the pandemic, most of the COVID-19 infections affected migrants who originated from malaria-endemic areas. This posed additional challenges in finding donors who were eligible to donate CCP.

An unexpected administrative difficulty that was faced initially was the lack of a service level agreement or memorandum of understanding between TTSH as a CCP supplier and other institutions with ill COVID-19 patients deemed appropriate for CCP infusion, as TTSH is not the blood establishment that supplies routine blood products to these institutions. All the stakeholders subsequently agreed that the CCP supplied by TTSH should not be subjected to the standard administrative requirements for routine blood products and would be best regarded as an urgent blood product needed for a serious life-threatening infection.

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## United States – American Red Cross

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### Question 1

- Type of institution
  - **National Blood Establishment** (responsible for any aspect of the collection, testing, processing, storage, release and/or distribution of human blood or blood components). Including recruitment of donors, screening and selecting blood donors.
- Institution demographics
  - Approximate number of whole blood and apheresis collections made/year for RBCs, platelets and plasma (as applicable). American Red Cross collects 4.4 million WB, 1.4 million apheresis collections

### Question 2

Every 7 days for a maximum of 8 times over 3 months. Routine plasma apheresis donors can donate every 28 days. There is no maximum number of donations for them over the year but their plasma volume loss is tracked and we have an upper limit for that.

Yes.

They are labelled as routine. These are our general donors who are coming in to donate because they fully qualify as a blood donor. If we were not doing COVID-19 antibody testing we would not even know these people had SARS-CoV-2 antibodies. Thus, the RBC products manufactured are labelled similar to any manufactured RBC from WB donation.

### Question 3

Transfusion for both compassionate use and clinical trials.

### Question 4

Yes. PCR, antigen and SARS-CoV-2 antibodies all qualify. 2 weeks from last day of symptoms associated with COVID-19

### Question 5

No.

### Question 6

If yes, please describe the test method and the cut-off criteria for accepting the donor for donation. Ortho total Ig test. A reactive test qualifies the unit.

*Question 7*

Ortho total Ig for spike 1 protein. A reactive test is permissible for labelling as CCP.

Yes.

*Question 8*

No.

*Question 9*

Not for 3 months following transfusion.

*Question 10*

Yes. Two weeks from last date of symptoms.

*Question 11*

Three months after transfusion

*Question 12*

The challenge has always been recruiting and retaining appropriately qualified donors. Most hospitals want to transfuse ABO matched plasma. Finding sufficient AB and B donors has been challenging.

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**Finland**

Jarkko Ihalainen & Antti Vierikko

*Question 1*

Finnish Red Cross Blood Service is the only Blood Establishment in Finland. Our laboratory and production are located in Helsinki where also our sole apheresis clinic resides. We collect and process whole blood from the whole country with 11 permanent offices and mobile drives.

Blood collection in Finland is being adjusted according to demand of red cells primarily and it has been diminishing slowly for the last 10 years. Currently we perform little less than 200 000 whole blood collections/year. We do not collect plasma with apheresis with the exception of a few units of IgA deficient plasma/year. Platelet apheresis is performed for HLA/HPA typed units and to maintain stocks in special situations. The number of thrombapheresis/year is ca. 2500, little more than 10% of collections.

*Question 2*

We only collect CCP with apheresis. We set up the procedure based on the plasmapheresis for IgA deficient plasma on our Terumo BCT Trima Accel v6.0 machines. We also configured the CCP product in our newly implemented Microsoft CRM/AX based blood establishment IT system with ICCBBA/ISBT codes, which were slightly adjusted, to our process needs. The products are labelled as CCP COVID-19 and in addition they are labelled for "research use only" because we only deliver to a clinical trial which has its own specifications for the products.

Our donors come from Helsinki University Central Hospital/University of Helsinki clinical research protocols for COVID-19 follow-up, i.e. all our donors are clinical trial participants as well as blood donors. We have set the maximal number of donations to five and the minimum interval between donations to 2 weeks (14 days). Only one donor so far has donated four times and the donation interval has generally been above two weeks. Since we only perform 1–3 plasmapheresis per year in normal circumstances all of this was new.

*Question 3*

Our CCP programme was built together with a clinical research group in Helsinki University Central Hospital. There has not been significant interest in CCP from other hospitals in Finland. Combined with the recommendations from the EU Commission, our local Competent Authority (Fimea) and WHO this cooperation made it clear that we only provide CCP for a clinical trial, which has not yet been registered to EU Clinical Trials Register. No compassionate or monitored use has occurred in Finland. We do neither currently have an agreement with industry on providing plasma for hyper-Ig production.

*Question 4*

Our CCP donors need to be eligible for donation according to our routine blood donor criteria. In addition, all of them come from follow-up cohorts who have had a PCR-confirmed COVID-19 infection and their recovery has been controlled and documented. We accept both female and male donors; the females are tested for anti-HLA-antibodies before donation.

*Question 5*

At first, we required negative COVID-19 PCR for eligibility but later this was changed to 14 days post full recovery. This is practicable since the donors come from follow-up cohorts so the timeline of recovery has been documented.



### Question 6

Our research collaborators tests the recovered patient cohorts and they target the invitations to participate in CCP donation research according to nAb levels. The research group laboratory uses an in-house microneutralization assay [14] [1].

### Question 7

In addition, we send aliquots from the donated CCP units to be tested by our collaborators and re-invite persons who have maintained adequate nAb levels. However, nAb levels are not used as a release criteria for our units as long as they only go to the clinical research project which is randomized and double-blinded for no plasma or high or low nAb concentrations.

### Question 8

Pathogen reduction/pathogen inactivation has not been our routine and we have not implemented it for CCP.

### Question 9

So far, no CCP transfusions have taken place in Finland so this question has not been completely solved. In principle, normal rules for donor health and transfusion requirements would be followed in addition to the CCP donor requirements.

### Question 10

We accept donors recovered from COVID-19 after 28 days in mild cases and 3 months after hospital treatment if they fulfil the other criteria. Quarantine after transfusion is 4 months so in practice this would be the limiting factor in these cases.

### Question 11

As in question 10, we accept the recipients of CCP according to the normal donor rules, in practice at a minimum of 4 months after the transfusion.

### Question 12

Early in the pandemic when we started the CCP project we had problems in getting apheresis collection sets from the manufacturer. In addition, we were in the final stages of implementation of our new blood establishment IT system, which took a significant part of the personnel resources. Later we have had problems with the two-way

clinical trial setting since both our donors and the recipients of CCP are participants in clinical trials. This has meant delays with several updates and Ethical Board applications for the protocols according to the cumulating clinical data and research findings. Finding an adequate number of donors in all blood groups is still a challenge. We have decided to stick to the ABO compatibility rules even though also cross-ABO protocols have been published (Focosi and Farrugia 2020) [2].

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## China

Yan Qiu, Ru Yang & Hua Xu

### Question 1

- Type of institution
  - *Regional Blood Services/Blood Centres*
- Institution demographics

The WB collection requirements for blood donor are the same all around the nation. The volume of WB collection can be 200ml, 300ml and 400ml, excluding anticoagulant and samples for test, which be selected by WB donors voluntarily during the pre-donation questionnaire. In China, the volume of 1 Unit (U) WB is 200 ml, namely 1 U = 200 ml.

According to the national regulation, the apheresis mainly collects the single donor platelets, while RBC and plasma are barely collected by apheresis in China. But 1 platelet apheresis procedure may produce 1 therapeutic unit (TU, 1TU =  $2.5 \times 10^{11}$  plts) PLTs, 1.5 TU PLTs, 1TU PLTs plus 2 U plasma or 2TU PLTs. The PLTs apheresis strategies vary among blood services with the equipment used.

- BRCBC
  - WB collections was approximate 450 000 U/year and apheresis collections was 68 000 TU/year for platelet and 3000 U for plasma.
- WHBC
  - WB collections was approximate 350 000 U/year and apheresis platelet was 70 000 TU/year.
- SXBC
  - WB collections was approximate 320 000 U/year and apheresis platelet was 40 000 TU/year

In the early February 2020, the national health authority issued a notice on Treatment COVID-19 patients with CCP affiliated a guideline for CCP collection. The guideline noted that the local COVID-19 patient designated hospitals were responsible for mobilization and recruiting CCP donors. The local blood centre implemented the CCP collection and preparation [1]. The detail of process varied among blood centres. For BRCBC and SXBC, the CCP collection were carried out in a blood donation mobile which equipped to ensure the safety of CCP donor, staff and the public. For WHBC, the CCP collection performed at 5 separated sites from the voluntary blood donation sites. The personal protection, disinfection and operation were taken strictly following the recommendations.

### Question 2

Only *plasmapheresis* is collected in China. CCP collection was performed following the plasma collection instruction of plasmapheresis procedure. The CCP donation interval is no less than 14 days and no more than 24 times a year, which is the same as the mandatory requirements of platelets apheresis by national guide for voluntary donors. In fact, the ratio of the repeat CCP donors is lower than that of regular blood donors from BRCBC and SXBC.

### Question 3

Generally the CCP was collected intend for *transfusion*. BRCBC and SXBC collected CCP only for prescription treatment-use. WHBC for trial use in the early stage, later for prescription treatment-use.

### Question 4

The CCP donor eligibility criteria:

- (1) diagnosed with COVID-19;
- (2) met the criteria of both disisolation and hospital discharge, including temperature returned to normal more than 3 days, respiratory symptoms improved significantly, pulmonary imaging showed significant improvement in acute exudative lesions, negative nucleic acid test (NAT) for two consecutive

respiratory specimens (nasopharyngeal swab sampling time at least 24 h. apart);

- (3) had recovered from COVID-19, no COVID-19 symptoms and had been discharged from the hospital for more than 2 weeks;
- (4) it is at least 3 weeks after the onset of symptoms prior to CCP donation [2];
- (5) qualification for blood donation health examination requirements, such as aged 18–55 years; weight should be more than 50 kg for male, and 45 kg for female. Alanine transaminase (ALT) testing result was below 40 IU/L. HIV Ag/Ab, anti-HCV, anti-syphilis, and HBsAg were all negative; NAT for HIV, HBV, and HCV were negative [1].

In addition for WHBC, they preferred to select CCP donors who had a fever lasting more than 3 days or a body temperature exceeding 38.5°C (101.3°F), and who intended to donate 4 weeks after the onset of symptoms [3,4].

Yes, SARS-CoV-2 ID-NAT must be negative for blood sample; anti-SARS-CoV-2 IgG antibody titre  $\geq 1:160$  or the qualitative test of the anti-SARS-CoV-2 total antibodies in serum/plasma is reactive and the test is still positive after the 320-fold dilution according to "Clinical treatment plan of convalescent plasma from recovered COVID-19 patients" [1].

The definition of recovery for donor eligibility criteria were stipulated in the "Diagnosis and Treatment of New Coronavirus Pneumonia" [2], and clinicians make judgments based on these regulations.

### Question 5

Not for BRCBC and SXBC which had no capability to conduct SARS-CoV-2 NAT which must be carried out in qualification Lab approved by certificate authority. Before the blood donation registration, the clinical hospital recruited the CCP donor and tested SARS-CoV-2 through PCR to confirm clearance of the infection and conveyed the results to blood centre.

But WHBC performed real-time reverse transcription PCR (RT-PCR) for SARS-CoV-2 RNA by using MultiScreen Pro RT-PCR assay (SYM-BIO LifeScience, they performed pool testing by mixing 6–8 plasma samples or individual testing by using 1.6 ml of plasma, eluting 100  $\mu$ l of nucleic acid template and added 40  $\mu$ l of it to the RT-PCR mix [5].

### Question 6

The answer is no for both BRCBC and SXBC. BRCBC had send the samples to cooperated certificated Lab to detect SARS-CoV-2 NAT and anti-SARS-CoV-2. SXBC accepted the tested results from the hospitals, which recruited the

CCP donors for blood centre to collect plasma. Yes for WHBC.

The anti-SARS-CoV-2 antibodies were detected by enzyme-linked immunosorbent assay (ELISA), which the 96 well microplate coated with recombinant RBD or N polypeptides per well. The samples were 20 times diluted by the phosphate-buffered saline, after incubation, washing, enzymed, incubation, washing, then adding chromogenic reagent and termination solution, finally we observed the plates for the horseradish peroxidase reaction. The OD values were calculated by measuring the change in the absorbance at 450 and 630 nm using an automatic microplate reader. Results were reported as the S/CO value, calculated as the ratio of the OD value to the cut-off value. The sample S/CO value  $\geq$  cut-off value was considered reactive, otherwise non-reactive. Titres were reported as the highest dilution when the ELISA assay was still reactive [6].

#### Question 7

Yes.

The ELISA to measure the anti-SARS-CoV-2 antibodies. The anti-SARS-CoV-2 IgG titre  $\geq$  1:160 or the total antibodies titre  $\geq$  1:320 as baseline for accepting for transfusion.

BRCBC, WHBC and SXBC collected the samples at the end of apheresis for future assessment and study.

#### Question 8

Not for BRCBC and Yes for WHBC and SXBC.

In China, there is only Methylene blue (MB) light treated plasma disposal set get the license from SDA. The pathogen reduction treatment for plasma is still optional.

#### Question 9

No. We all do not. According to national "health examination requirements for blood donor", those who have received whole blood and blood components within 1 year cannot donate blood again.

#### Question 10

Yes.

We accept individuals who had recovered from COVID-19 and had been discharged from the hospital for more than 6 months for standard whole blood or platelet apheresis donation.

#### Question 11

Not yet at present.

As mentioned in answer to question 9, one year deferral for blood transfused recipients. Another reason is that it will take a long time to evaluate whether individuals recovering from COVID-19 infection have other potential health impairments, and whether they can recover or how long it will take to recover to normal. Therefore, it is still too early to discuss whether to accept individuals recovered from COVID-19 infection as normal blood donors. At present, according to the regulations, we will not accept it for at least five years.

#### Question 12

Lack of enough background knowledge of COVID-19 and protection measurement that are vital for staff.

No experience in collection and training of COVID-19 CCP in a short period time.

Prepare all the equipment, facilities under contingency situation.

The relative guideline updated frequently.

Set up rapidly good communication with the cooperated hospitals and other institutes.

It is very encouraging that the CCP donors in WHBC are very enthusiasm and half of them become loyal repeat blood donors. WHBC had a donor who gave 13 consecutive donations!

Most of the CCP donors in WHBC's pilot program had an S-RBD-specific IgG titre of  $\geq$ 1:160. As time goes on, the antibody titres of different donors show differences. Some donors lost their antibodies very quickly; some of them lasted for more than half a year.

Whether the CCP effect will be reduced by the pathogen reduction treatment?

We all believe that the problem was resolved and the process was smooth under the great effort of blood people.

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## Israel

Naomi Rahimi-Levene, Eilat Shinar & Marina Izak

### Question 1

- Respondent demographics
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    - Institution (name): Magen David Adom National Blood Services
- Magen David Adom is a *National Blood Establishment* (responsible for any aspect of the collection, testing, processing, storage, release and/or distribution of human blood or blood components).
- The approximate number of whole blood and apheresis collections made/year for RBCs, platelets and plasma (based on 2019):

- 265 000 whole blood units, from them: 150 000 random donor platelet units were separated and 90 000 fresh frozen plasma units were separated.
- 1750 apheresis plasma units (each divided into 3 units of plasma).
- 550 units single donor apheresis platelet units.

### Question 2

- 2a. The donor is allowed to donate CCP every 2 weeks till anti N antibodies (Abbott, USA) level drops below S/CO of 4. No more than 6 times in a 100 days period.
- 2b. This differs from donation frequency for routine plasma by apheresis. Routine plasma donors are invited every 4 weeks.
- 2c. The plasma from Whole blood donors can be used as CCP if 28 days elapsed from the full recovery from COVID-19. The cellular components are labelled as regular components. This decision is based on the FDA/AABB and the Israeli Ministry of Health regulations.

### Question 3

CCP is collected both for compassionate use and for trial use.

### Question 4

- 4a. SARS-CoV-2 PCR test is acceptable for CCP donor eligibility.
- 4b. Donor eligibility for CCP is 14 days following recovery with 2 negative SARS-CoV-2 PCR test results or a letter from the treating physician stating full recovery.

### Question 5

No, the donor is not tested for SARS-CoV-2 by PCR before donation to confirm clearance of the infection.

### Question 6

Yes. We perform a Point of Care rapid test by lateral flow that detects anti S antibodies (PharmaAct, Germany) to avoid collection of CCP with donors with no-detectable antibodies.

### Question 7

7a. We use Abbott SARS-CoV-2 anti N on each donor. The CO is 1.4. Only units with antibodies levels above S/CO of 4 are used for transfusion and units with antibody levels above 1.4 are used for fractionation.

7b. We also archive samples for future tests.

7a. We use Abbott SARS-CoV-2 anti N on each donor. The CO is 1-4. Only units with antibodies levels above S/CO of 4 are used for transfusion and units with antibody levels above 1-4 are used for fractionation.

7b. We archive samples for future tests.

#### Question 8

No, CCP is not subjected to a pathogen reduction treatment.

#### Question 9

Recipients of CCP for convalescent plasma donation are accepted only 6 months post-transfusion.

#### Question 10

Individuals recovered from COVID-19 infection are accepted for standard whole blood or apheresis (platelet or plasma) donation after 28 days.

#### Question 11

Recipients of CCP for standard whole blood or apheresis (platelet or plasma) donation are accepted after 6 months post-transfusion.

#### Question 12

The challenges faced and lessons learned from establishing a CCP collection program are to:

1. Set up a multi-disciplinary project, involving the Authorities, treating physicians, national blood services, hospital blood banks.
2. Provide potential donors with the information of the importance of donations of CCP, for the treatment of patients with moderate (and sometimes severe) COVID-19.
3. Perform POC quick antibodies test to avoid collection of CCP from people with no or low level of antibodies.
4. Provide CCP ASAP to the patients (no later than 72 h of physician request).

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### Argentina

Carlos Alberto Gonzalez, David Martin Ferrari & Paula Verónica Cini

#### Question 1

We work on a Hospital-based blood transfusion service with blood bank (a hospital unit responsible for blood collections, pre-transfusion and compatibility testing, and issuing blood for clinical transfusion exclusively for use within hospital facilities). Hospital de Infecciosas Francisco Javier Muñiz is a monovalent hospital; it serves only patients with infectious diseases.

The hospital has 421 beds, there are approximately 587 RBC's transfused/year (without pandemic) attending to both adult and paediatric patients. Patients admitted for medical or surgical reasons are treated. Our blood bank collects 600 blood donors per year.

#### Question 2

Our Institution performs CCP donation for plasmapheresis and whole blood, following the guidelines issued by our Ministry of Health of the Nation [1]. There are no differences in frequency regarding routine plasma donation by plasmapheresis.

A donor may be subjected to plasmapheresis up to 1 time every 2 weeks. In any case, the volume of plasma extracted per session should not exceed 600 ml (not counting the anticoagulant, i.e. about 650 ml of anticoagulated plasma), 1000 ml in a week and 15 litres in a year. Red blood cells concentrates and platelets obtained from whole blood donation from convalescent donors were used for standard transfusions because of the following main reasons. First, according to our donor eligibility criteria and literature, SARS-CoV-2 transmission by transfusion has not been demonstrated. Secondly, our recipients were all patients with COVID-19. Finally, the protocol was approved by our Institutional Ethics Committee. These components are labelled as convalescent donation. We always try that patients receiving multiple components receive those components from the same donor.

#### Question 3

From the beginning of the pandemic in our country, our institution has collected CCP for an institutional clinical trial (NCT04468009) [2] and an extended access protocol.

### Questions 4, 5, 10

The CCP donor eligibility criteria used in our institution changed according to the guidelines by the Ministry of Health of the Nation.

Since April 4th, people with a full resolution of symptoms at least 14 days prior to donation and 2 negative PCR SARS-CoV-2 tests performed with an interval of at least 24 h from nasopharyngeal sampling were accepted as donors. Since May 12th, people with a full resolution of symptom at least 14 days prior to donation with negative PCR SARS-CoV-2 (1 or 2) tests from nasopharyngeal sampling performed with an interval of at least 24–48 h were accepted as donors. Since July 2nd, people can be accepted to donate 28 days after symptom resolution (if a test has not been performed); at the same time, they can be accepted to donate 14 days after symptom resolution with a negative PCR SARS-CoV-2 test.

### Questions 6 and 7

For detection and titration of IgG anti-SARS-CoV-2 antibodies in blood donors, a manual enzyme immunoassay in microplate was performed at our institution. This assay (COVIDAR IgG, Conicet-Leloir Institute) uses the spike and RBD (receptor-binding domain) proteins as antigenic source corresponding to SARS-CoV-2 expressed in cell culture. The cut-off criterion was >160 until 19th October; since then, a titer >800 or R.P. > 4.0

### Question 8

We never used a pathogen reduction methodology in CCP.

### Questions 9 and 11

According to our national standards [1], all transfusion recipients can be accepted as blood donors after 1 year of being transfused.

### Question 12

The current pandemic is an extraordinary and unexpected event for blood services and has allowed us to learn some lessons.

In a very short time, we had to support the continuous training of physicians and technicians in biosecurity, ethics, good clinical practices and teleworking. According to the evolution of the pandemic and successive changes in the definitions of the Ministry of Health, the donor interview and the clinical trial CCP were regularly updated.

We had to learn how to make the operation of the service more flexible in order to adapt to a new context of public health. The changes that were usually implemented in a long time, we had to implement them in days or hours. In Argentina and because of the effects of the pandemic, the ASPO (Preventive and Mandatory Social Isolation) began on 20th March, which reduced the concurrence of blood donors by more than 90% in June and we managed to recover quickly in July by reaching and tripling the historical level of blood donation to our PCC-collection program. This was achieved by coordinating with other services of our institution that treat patients with COVID-19 so that once they recover, they invite them to donate plasma. More importantly, to facilitate the concurrence of donors an email address and cell phone ad hoc and social networks contact were implemented.

On the other hand, the pandemic shows the worst and the best of society. The worst accounts for the mass media and fake news. The best, the solidarity of our patients who spontaneously came to donate plasma, achieving a quick change of reposition donor (majority in our environment) to voluntary convalescent donor.

Finally, it is clearly that human resource is a critical and essential component in the management of health service. These continuous changes were possible in the light of the commitment of the members of the hemotherapy service.

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### Indonesia

Robby Nur Aditya

**Question 1**

- Type of institution
  - National Blood Services/Blood Centre** (responsible for recruiting donors; screening and selecting blood donors; blood collection; testing and processing blood units; transporting; receiving and storage of blood units; pre-transfusion testing, and issuing blood for clinical transfusion at a national level)
- Institution demographics
  - For blood establishments and blood services
  - Approximate number of whole blood and apheresis collections made/year for RBCs, platelets and plasma (as applicable)

We have collected 3 523 982 Whole Blood Donation in 2019

**Question 2**

Plasmapheresis.

If *plasmapheresis* is collected, how many times is a donor allowed to donate CCP, and over what time period?

Donor allowed to donate CCP between 3-6 times, every 2 weeks, and will depends on the antibody titre.

**Question 3**

For transfusion only.

Trial use.

**Question 4**

Requirements are:

- 18–60 years old
- Body Weight  $\geq$  55 kg
- History of positive swab with at least 1 negative result
- 14 days free of symptoms

SARS-CoV-2 PCR with Swab test.

14 days with no symptoms and negative result for PCR

**Question 5**

No.

**Question 6**

Yes, the test method is Rapid test with cut-off criteria is 1/80.

**Question 7**

Same with question 6.

Yes, samples will archived for future assessment.

**Question 8**

No.

**Question 9**

Yes.

**Question 10**

Yes.

14 days with no symptoms

**Question 11**

Yes.

1 year

**Question 12**

- Lack of donor to donate CCP due to social stigma
- 'Big hope' from patients and family for CCP treatments
- More education, information and socialization about CCP to community
- Apheresis or plasmapheresis more better known as an alternative donation for public

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**India – Chandigarh**

Ratti Ram Sharma, Suchet Sachdev, Rekha Hans & Divjot Singh Lamba.

**Question 1**

Type of institution.

Hospital-based Blood Transfusion Service/Blood Bank (a hospital unit responsible for pre-transfusion and compatibility testing, and issuing blood for clinical transfusion exclusively for use within hospital facilities).

Institution demographics.

For hospital (2019–2020).

Number of in-patient beds: 1740.

Approximate number of RBCs transfused/year: 1 35 685.

Age group of patients treated (neonates, paediatrics <18 years, adults >18 years): All age groups.

Type of patients treated (medical or surgical): Medical and Surgical.

For blood establishments and blood services (2019–2020). Approximate number of whole blood and apheresis collections made/year for RBCs, platelets and plasma (as applicable).

Whole blood collection: 57 842.

RBCs: 56 962.

Platelets: 26 460.

Plasma: 51 411.

### Question 2

Our institution performed Plasmapheresis for CCP donation.

- Most of the donors donated for single time, however few donors donated twice or thrice (one donor only) after an interval of more than 14 days of previous donation. The donation frequency did not differ from that permitted for routine plasma donation by apheresis.
- Whole blood was not collected for CCP donation at our centre.

### Question 3

CCP collected is intended for transfusion to the patients fulfilling criteria for convalescent plasma (Off Label) under Investigational therapies (Version 4, 27-6-2020) Ministry of Health and Family Welfare, India notification, or as updated from time to time. Initially, it was done as a part of PLACID trial (Clinical Trial Registry of India CTRI/2020/04/024775) and later for compassionate use also. Our institute started facility of plasma bank to support COVID-19 convalescent plasma therapy to the patients admitted in COVID-19 hospital facility of our institute as well as patients admitted in hospitals outside our institute.

### Question 4

Eligible donors are men or nulliparous women with age between 18 and 65 years, weight more than 50 kg, were diagnosed COVID-19 by confirmed RT-PCR test result and had experienced symptoms of COVID-19 with at least fever and cough. Additionally, the symptoms must have completely resolved for 28 consecutive days before donation or a period of 14 days before donation with two negative RT-PCR test results for SARS-CoV-2 from nasopharyngeal swabs collected 24 h apart. All routine screening tests, including ABO blood grouping and antibody screening; Rh D phenotype; complete blood counts; screening for HIV, hepatitis B or C virus, syphilis, and

malaria; and total serum protein were conducted as per Indian Council of Medical Research protocol for convalescent plasma use in COVID-19 patients version 1.5 dated 11th May 2020 being followed and donor eligibility criteria for whole blood donations in accordance to the Drugs & Cosmetics Act 1940 and rules 1945 therein (as amended till March 2020 [1]).

Yes, our donors need to have a confirmatory test result status of past COVID-19 infection before CCP donation.

- RT-PCR test results for SARS-CoV-2 from nasopharyngeal swab is considered acceptable.
- Complete resolution of symptoms for 28 consecutive days before donation or a period of 14 days before donation with two negative RT-PCR test results for SARS-CoV-2 from nasopharyngeal swabs collected 24 h apart and reactivity for SARS-CoV-2 IgG by Chemiluminescence method was tested for recovery in our donors.

### Question 5

No, our institution does not test the CCP donor for SARS-CoV-2 by PCR before donation to confirm clearance of the infection.

### Question 6

Testing of SARS-CoV-2 antibody by Chemiluminescence method (Ortho Clinical Diagnostics) with a minimum acceptable signal-to cut-off ratio of  $\geq 13.0$  as per guidelines of Indian council of medical research (ICMR), under Ministry of Health and Family Welfare, Govt. of India and protocol for convalescent plasma use in COVID-19 patients version 1.5 dated 11th May 2020 being followed and subsequent Evidence Based Advisory to address Inappropriate Use of Convalescent Plasma in COVID-19 Patients by ICMR dated 17/11/2020.

### Question 7

No, not tested as of now but the samples are being collected from CCP unit and being frozen for future assessments.

### Question 8

CCP was not subjected to any pathogen reduction.

### Question 9

No, until 1 year, CCP/Blood or Blood component recipients are deferred from routine blood donations and convalescent plasma donations as per ICMR protocol for



convalescent plasma use in COVID-19 patients version 1.5 dated 11th May 2020 being followed and donor eligibility criteria for whole blood donations in accordance to the Drugs & Cosmetics Act 1940 and rules 1945 therein (as amended till March 2020 [1]).

#### Question 10

Yes, they are accepted for whole blood and platelet donations after they have completely recovered from COVID-19 infection. Minimum deferral period after recovery is 28 days.

#### Question 11

No, until 1 year, CCP/Blood and blood component recipients are deferred from routine blood donations as per ICMR protocol for convalescent plasma use in COVID-19 patients version 1.5 dated 11th May 2020 being followed and donor eligibility criteria for whole blood donations in accordance to the Drugs & Cosmetics Act 1940 and rules 1945 therein (as amended till March 2020 [1]).

#### Question 12

1. The information, education and communication to motivate convalescent plasma donors was a challenging task for the Transfusion services that were already grappling with issues of motivating and recruiting enough whole blood donors to meet the blood and blood component demands of patients coming to us with non-COVID indications such thalassaemia, pregnant women, cancers and other medical and surgical emergencies.
2. The arrangements of logistics for blood donors transport, critical supplies for testing blood and the extra measures that were instituted for maintain safety of the blood donors and the staff.
3. The donors were not having knowledge about convalescent plasma donation when they were under medical supervision in designated hospitals or quarantine centre's or when they were being tele-counselled about the do's and don'ts about the corona virus disease 2019 (COVID-19).
4. Donors were hesitant to come to hospital-based blood centres for the plasma donation, as they were apprehensive about the fact that their immunity will be weakened, and may be susceptible to infections (COVID and Non-COVID).
5. Donors had residual issues after recovering from COVID-19, in form of generalized weakness, muscle pains, residual cough, shortness of breath on mild

exertion etc. Donors having any of these symptoms were excluded from the CCP Donation.

6. Many COVID-19 recovered patients were asymptomatic and did not have explicit symptoms suggesting a systemic immune response like fever. Whereas others of age less than 18 or greater than 60 years and multiparous females were not included as potential plasma donors.
7. Donors, who were initially willing, were finally not available as they were mostly struggling to step up daily routine due to the financial and business disruption caused by the pandemic.
8. Many potential donors were not fit to be included in the program due to reasons like uncontrolled DM/HTN, low haemoglobin, deranged Liver Function Tests and significant weight loss.
9. Initially there was no clear consensus on IgG antibodies cut-off for the different testing platforms (ELISA, CLIA, Enhanced CLIA, Electrochemiluminescence), later the national guidelines provided signal-to-cut-off ratio of  $\geq 13.0$  for prospective CCP donor eligibility.
10. The lesson learnt was the need for a dedicated donor recruitment cell in the blood centre with tele calling facility to motivate whole blood and plasma donors as part of the disaster management plan of the blood centre.

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## Norway

Lise Sofie H. Nissen-Meyer.

### Question 1

- In Norway, a national cooperation (NORPLASMA COVID-19 [1]) uniting all the major regional/hospital-based blood services was established in April 2020 in an effort to provide CCP to patients. The project applied national rules in coherence with European guidelines, for collection, testing and storage of CCP. Recently, an initiative to test anti-SARS-CoV-2 for all collected units on one platform has been taken. In addition to production and testing of CCP, the project also includes design of clinical studies to evaluate effect of CCP treatment in patients. The description provided here thus includes all blood centres participating in the national project.

#### ○ Institution demographics

Altogether, Norwegian blood banks collect ~175 000 whole blood units per year (2018) and perform 16 000 apheresis procedures (2000 RBC, 5,000 TRC, 9000 plasma). We serve all the hospitals in the country and all types of patients are treated.

### Question 2

Norwegian blood banks collect CCP through plasmapheresis, thrombapheresis procedures and from whole blood.

Collection by plasmapheresis is allowed 4 times over at least 4 weeks as long as the donor is eligible for donation. This is more often than our regular plasma donation frequency (monthly or twice a month).

When plasma is collected from whole blood donations, the derived RBCs and platelets are used for standard transfusions. This was decided based on the guidelines from ECDC/EBA, recommending that all donors are quarantined >4 weeks following recovering from COVID-19 illness or positive PCR test before allowed to donate whole blood. Since no transmission of SARS-CoV-2 has been shown, this is considered safe. The products (apart from plasma) are not labelled in any specific way.

### Question 3

In Norway, collected CCP is intended for transfusion if it contains a sufficient amount of antibodies, and if not, the plan is to use the plasma for fractionation.

The intention for collection of CCP is both compassionate use and trial use. In Norway, we have not succeeded in obtaining financial support for an RCT, therefore, the use we have had this far is only compassionate use. However, all patients are asked to join a monitoring study to collect

data to evaluate the treatment, as recommended in EU/EBA guidelines.

### Question 4

All CCP donors have to fulfil the eligibility criteria for ordinary blood donors in Norway.

Towards the end of the year, the donors need to have a confirmatory test result before CCP donation. In the springtime when testing was limited to very strict criteria, we collected plasma from some donors based on anamnestic information, and a majority of these had antibodies.

At present, either a positive PCR test at the time of infection, or a positive antibody test later, is considered acceptable. Antibody levels are being measured at every donation.

Recovery is defined by the absence of acute symptoms including fever, cough, other upper airway symptoms, headaches. Prolonged loss of smell/taste or intermittent, short episodes of fatigue are not deferral reasons in itself, if the donor feels generally recovered and is back in normal routines.

### Question 5

In Norway, we do not test the donor by PCR before donation to confirm clearance of SARS-CoV-2 infection. All donors are quarantined for 28 days following recovery as described in Q4.

### Question 6

In Norwegian blood centres, some donors are tested for anti-SARS-CoV-2 antibody levels before donation, but most are tested in connection with donation and the decision to use CCP is taken later.

We have recently agreed to use an in-house test showing inhibition of binding to the ACE2-receptor as the national test method for CCP, with a cut-off which has not been finally calculated yet but most likely will be somewhere around 60%.

### Question 7

CCP units are tested for anti-SARS-CoV-2 antibodies using at least two of the following: total antibody testing (Commercial tests from different providers), in-house multiplex tests developed with peptides to bind anti-RBD and anti-nucleocapsid protein, inhibition of binding to ACE2 and conventional neutralization testing of selected units. Final cut-off values have yet not been established. In the initial phase, we have used a combination of

antibodies against RBD and nucleocapsid as release criterion. When data from inhibition and neutralization assays now is available, the release criterion will be changed accordingly. In addition, samples collected from all CCP units are frozen/archived for future assessment.

#### Question 8

CCPs are not subjected to a pathogen reduction treatment. The prevalence of transfusion-transmitted infectious agents is very low in Norway, and the use of only approved blood donors further contributes to product safety.

#### Question 9

No recipients of CCP have offered to donate convalescent plasma yet, but the decision whether such person could donate plasma would depend upon the general eligibility for blood donation of this person (see question 11).

#### Question 10

Norwegian blood banks accept individuals recovered from COVID-19 infection for standard whole blood or apheresis (platelet or plasma) donation following a recovery time of at least 28 days.

#### Question 11

Recipients of CCP can be accepted for donation of standard whole blood or apheresis if they are otherwise eligible as regular blood donors. However, according to Norwegian rules, receiving an allogeneic transfusion elicits a minimum deferral period of 6 months.

#### Question 12

The most challenging part of establishing a CCP collection program has been to develop and validate testing methods. This is time-consuming and depends on strong collaboration with the laboratory developing the tests. Also, the handling and separate workflow concerning these donors have been challenging, as all requirements for regular blood donation and transfusions had to be met. Lastly, the blood banks did not receive additional resources to implement the CCP program. However, knowledge and experience have been gained and we are probably better prepared for a new pandemic.

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### Canada – Canadian Blood Services, Vancouver

Dana V. Devine.

#### Question 1

- Type of institution
  - National Blood Service
- Institution demographics
  - For blood establishments and blood services
  - Approximate number of whole blood and apheresis collections made/year for RBCs, platelets and plasma (as applicable): In fiscal year 2019–2020, Canadian Blood Services collected 763 319 whole blood units, 126 277 platelet doses of which 21 493 were apheresis platelet collections in 11 339 individual apheresis procedures, and 48 610 plasma collections made either as specific apheresis plasma collections or collected concurrently with a plateletpheresis procedure.

#### Question 2

Canadian Blood Services stood up its CCP program in April 2020. Plasma is collected only by plasmapheresis. Donors who have appropriately high titres of neutralizing antibodies are requested to donate as frequently as once a week. This is the same donation frequency permitted for routine plasma donation.

#### Question 3

In Canada, CCP is collected primarily for use in three clinical trials. The regulatory authority, Health Canada, has provided a mechanism by which a physician could request an 'n = 1' clinical trial to treat an individual patient. Perhaps due to the paperwork burden of obtaining a clinical trials authorization for a single patient, there have been no requests for 'n = 1' studies, and all CCP collected has been used in national clinical trials. At this point, all CCP is intended for transfusion although discussions about supporting hyperimmune globulin production are ongoing.

#### Question 4

In addition to meeting all donor eligibility criteria that are applied to regular plasma donors, CCP donors must

have evidence of a RT-PCR positive SARS-CoV-2 test or be presumptive positive. The latter means that the donor resides in a household with someone who tested positive by RT-PCR and was sick with COVID symptoms at the same time. In addition, donors must be 28 days past resolution of symptoms prior to donation.

#### Question 5

Donors to the Canadian Blood Services CCP program are not tested for virus as there is little evidence that viral material is still in the circulation 28 days after resolution of symptoms, and no evidence to date that virus in blood is infectious.

#### Question 6

Donors are not tested for antibodies prior to donation; rather we rely on a confirmed virus test or presumptive positivity based on symptoms and cohabitation with an individual who was test positive.

#### Question 7

All donations are tested for anti-SARS-CoV-2 neutralizing antibodies. The test is a plaque reduction neutralization test (PRNT) using Vero E6 cell cultures and live SARS-CoV-2. Those donations with a PRNT<sub>50</sub> titre of  $\geq 1:160$  are released for clinical trial use. Donors with titres of 1:80 are encouraged to return for a subsequent donation; owing to the variability in the PRNT assay subsequent donations may return to 1:160 or greater. Samples are retained for subsequent testing on various antibody testing platforms.

#### Question 8

CCP used for clinical trials in Canada is not subjected to any pathogen inactivation technology. This is also true of regular transfusion plasma.

#### Question 9

We have not faced this particular situation; however, given the relatively short time that donors maintain adequate antibody titre, it would be unlikely. Any recipient of a blood product is deferred for 6 months.

#### Question 10

Yes, donors who have recovered from COVID-19 may donate blood or plasma as long as they are at least 21 days past resolution of their symptoms.

#### Question 11

Donors who had received CCP would be accepted for donation, but only after a 6-month deferral for receipt of a transfusion product.

#### Question 12

The main challenge in setting up a new program to collect COVID convalescent plasma was doing so in the midst of the pandemic when our organization was trying to cope with the installation of COVID safety precautions including masking and physical distancing which slowed down clinic operations. The need to maintain the blood supply is paramount, so the CCP program set up had considerable involvement from research & development staff members who could be diverted to this work. The main challenge in ongoing program operation has been recruitment of donors. Many of the recovered COVID patients are new to blood or plasma donation; only 4% of eligible Canadians donate blood so there is minimal overlap between the population of blood donors and the population of COVID patients. While we had good media coverage of CCP early in the pandemic (March-May), it has been difficult to attract sufficient donors with high titre antibodies during the second wave. This has led to challenges supporting the national clinical trials of CCP that are ongoing in Canada. Novel recruiting strategies and the involvement of institutions and physicians caring for COVID patients has been key to the recruitment of new donors.

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#### Hong Kong

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#### Question 1

**Regional Blood Services/Blood Centre** (responsible for recruiting donors; screening and selecting blood donors; blood collection; testing and processing blood units; transporting; receiving and storage of blood units; pre-transfusion testing, and issuing blood for clinical transfusion at a regional level)

- Institution demographics

Around 215 000 whole blood collection and 10 000 apheresis collections for platelets and plasma per year

*Question 2*

Eligible donors are invited to donate up to 6 times of plasmapheresis.

The donation frequency is the same as that for routine plasma donation i.e. with donation interval of at least 14 days apart.

*Question 3*

Both, for clinical study use at the beginning, mostly for compassionate use now.

*Question 4*

Yes, all recovered patients must have SARS-CoV-2 PCR confirmed positive at diagnosis and recovered with at least two SARS-CoV-2 PCR negative before discharge. In addition, they must have neutralizing antibodies titre  $\geq 1:80$  before referral for convalescent plasma donation.

All donors have to be fully recovered from the SARS-CoV-2 infection as documented by negative NPS RT-PCR for SARS-CoV-2 four weeks before donation and negative NPS and serum RT-PCR for SARS-CoV-2 within 1 week of the donation.

*Question 5*

No, as response to Question 4, recovered patients were confirmed full recovery from COVID-19 and demonstrated to have sufficient neutralization antibodies titres.

*Question 6*

Yes, sufficient titre of neutralization antibodies were required to be eligible.

*Question 7*

An in-house live virus neutralizing antibody assay. Samples are collected from the CCP unit and sent to the university for further assessment.

*Question 8*

No.

*Question 9*

Not decided but unlikely as (1) most CCP recipients were elder and (2) the number of patients received were still small locally.

*Question 10*

Recovered patient would only be accepted for whole blood or apheresis donation at 180 days after he/she completely recovered from COVID-19 infection and passed the health screening assessment required by our institution.

*Question 11*

Only at 12 months after the last transfusion event.

*Question 12**CCP donors*

It is observed that majority of referred CCP donors never donate blood before and they have little idea on blood donation and virtually none on apheresis donation. The frontline staff have to spend more time to introduce the apheresis donation and explain the procedures in detail.

As the CCP donors were just recovered from the COVID-19, they most have concerns on their health after the COVID-19 infection. Some also expressed their worries and myths about apheresis plasma donation, such as plasma donation would reduce their antibody titre to a level not enough to provide protection against subsequent infection. The professional staff has to reassure them to ease their concerns and explain how they could help other critical patients. Nevertheless, some CCP donors accepted and joined the program but some still had hesitation and withdrew.

*Infection control concerns*

Initially some staff and public have concerns of contamination from the potential reactivation of COVID-19 infection of the CCP donors. A separated room was then prepared for the CCP donation. As the CCP donors have repeatedly negative SARS-CoV-2 PCR results and with reassurance given to staff and public, they were donated at one end of the same apheresis suite.

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## France

Pierre Tiberghien, Pierre Gallian & Pascal Morel

### Question 1

- Type of institution
  - *National Blood Establishment*
  - 2019: 2.5 million whole blood donations, 440 000 apheresis (340 000 plasma apheresis, 99 000 plasma/platelet apheresis, 1000 other apheresis)

### Question 2

It does not differ. Policy for standard plasma apheresis is applied (at least 2 weeks between 2 plasma donations, and no more than 24 donations by year).

Whole blood is not collected for convalescent plasma collection.

### Question 3

CPP is collected for transfusion: both trial use and compassionate use. Collection of CCP for plasma fractionation is being considered.

### Question 4

No. Of note, during the first COVID-19 peak in March and April 2020 patients with mild clinical signs were not systemically tested by RT-PCR and diagnosis was essentially symptomatic.

Absence of clinical signs since at least 14 days.

### Question 5

No.

### Question 6

No.

### Question 7

All CCP are screened by an ELISA assay for the detection of IgG anti-SARS-CoV-2 according to the manufacturer instruction (ELISA SARS-CoV-2 (IgG); Euroimmun). CP units with a ratio  $\geq 8$  (earlier  $\geq 5,6$ ) are accepted for use as convalescent plasma. CP units with a ratio  $\geq 1,6$  (earlier

1,1) and  $< 8$  (earlier 5,6) are further tested for neutralizing activity and accepted for use as convalescent plasma in the presence of a titre  $\geq 80$  (earlier  $\geq 40$ ). Neutralizing activity is assessed using live SARS-CoV-2 virus, as described Gallian et al. [1].

Yes.

In addition, CCP are qualified according the usual requirements for blood products. Also, individual HEV NAT screening is performed.

### Question 8

Yes, all CCP are treated by amotosalen + UVA (Intercept Blood System) according to the manufacturer instruction.

### Question 9

No. French regulations do not allow collecting blood from individuals with history of transfusion.

### Question 10

Individuals who recovered from COVID-19 are accepted for blood donation 28 days after the end of clinical signs. In addition, patients with history of hospitalization in intensive care unit are deferred 4 months.

### Question 11

No. French regulations does not allow to collect blood from individuals with history of transfusion.

### Question 12

Strengths included donor implication, EFS personal mobilization, reactive interactions with regulatory authorities, efficient messaging towards the donors, strong productive interactions with academic/research teams, plasma apheresis availability in most fixed collection sites, availability of pathogen reduction technology, and supportive European institutions (ECDC, DG Santé/European Commission). Weakness and challenges included difficulties to develop a dedicated IT-supported process for CCP collection, manufacturing and testing, occasional competition for resources between whole collection and convalescent plasma collection, introducing novel (and evolving) testing as well as occasional limited personal availability in the midst of an evolving crisis.

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## Oman

Arwa Z. Al-Riyami, Khuloud Al Maamari & Zaid Al-Hinai

### Question 1

- Type of institution
  - **Hospital-based Blood Services** (a hospital unit performing the functions of blood establishment and transfusion services at a hospital level)
- Institution demographics
  - For hospital
    - Number of in-patient beds: 450
    - Approximate number of RBCs transfused/year: 18 500
    - Age group of patients treated (neonates, paediatrics <18 years, adults >18 years): all
    - Type of patients treated (medical or surgical): both
  - For blood establishments and blood services
    - Whole blood collection: 12 500
    - Platelet apheresis collection: on-demand; approximately 50 platelet apheresis procedures/year

### Question 2

Our institution has established a CCP donation program by plasmapheresis only.

Donors are allowed to donate CCP by plasmapheresis up to four times; seven days apart, if tolerated the procedure well.

Our institution did not collect plasmapheresis from regular donors before the establishment of the CCP collection program.

Our institution does not collect CCP from whole blood donations.

### Question 3

CCP collected in our institution for transfusion purposes for trial use only.

### Question 4

Yes. A confirmatory status of past COVID-19 infection (SARS-CoV-2 RNA by RT-PCR or anti-SARS-CoV-2 IgG antibody) in the donor is a pre-requisite. In addition, all CCP donors undergo testing for anti-SARS-CoV-2 IgG antibody levels before scheduling an appointment for plasmapheresis.

Recovery is defined as:

- Resolution of fevers for > 72 h, and
- Improvement in respiratory symptoms, and
- Passage of >7 days since onset of the symptoms.

### Question 5

Yes, donors who have complete resolution of symptoms by at least 14 days and before 28 days are tested for SARS-CoV-2 RNA by RT-PCR on a nasopharyngeal swab specimen at the time of donor screening.

If a donor presented for donation beyond 28 days from the time of complete resolution of symptoms, testing for SARS-CoV-2 RNA PCR is not performed.

Donors are allowed to donate CCP if any of the following:

- Complete resolution of symptoms at least 14 days before donation, AND negative results for SARS-CoV-2 RNA on a nasopharyngeal swab specimen.
- OR
- Complete resolution of symptoms at least 28 days before donation without SARS-CoV-2 RNA testing
- The plasmapheresis appointment is decided based on the time of resolution of symptoms, and the results of the SARS-CoV-2 RNA RT-PCR at the time of donor screening (as above)

### Question 6

Yes, donors are tested for anti-SARS-CoV-2 IgG antibodies at the time of donor screening before plasmapheresis. Testing is performed using EUROIMMUN® ELISA assay (Lübeck, Germany). A signal-to-cut-off ratio  $\geq 2$  is considered acceptable for donation.

**Question 7**

Yes. Testing of anti-SARS-CoV-2 antibodies on the CCP units is performed using EUROIMMUN® ELISA assay (Lubeck, Germany). A signal-to-cut-off ratio  $\geq 2$  is considered acceptable for unit transfusion/use.

Yes. Additional samples are collected from the CCP unit and frozen for future testing for neutralizing antibody titres.

**Question 8**

Yes, Collected CCP is subjected to pathogen inactivation via the Mirasol Pathogen Reduction Technology System (Terumo BCT).

**Question 9**

No. Recipients of CCP are temporarily deferred from all types of blood donation including CCP donation for a minimum of one year. Hence, they will not be eligible to donate CCP within the timeframe of the conducted trial.

**Question 10**

Yes. Our institution accepts individuals who recovered from COVID-19 infection for blood donation minimum of 28 days after a resolution of symptoms and cessation of therapy.

**Question 11**

Yes. Our blood services accept recipients of CCP for standard whole blood and apheresis donation if they meet other donation criteria and after a temporary deferral period of a minimum of 1 year.

**Question 12**

Challenges faced:

Managing a new apheresis service at the time of shortage of staff during the pandemic.

Accommodating CCP donors along with the regular blood donors with existing space limitation in the donation centre, and at the time of undertaking COVID precautionary measures including social distancing. We, therefore, opted to perform CCP plasmapheresis procedures outside the regular blood service's working hours.

Recruiting CCP donors of certain blood groups such as group A, B and AB, considering that group O is the commonest blood group in the population.

Lessons learned:

To initiate clinical trials early in the pandemic to enable recruitment of the required number of patients and before the decline in number of cases.

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**Netherlands – Sanquin**

Hans Vrieling & Cynthia So-Osman

**Question 1**

- Type of institution
  - Sanquin Blood Supply: *National Blood Establishment* of the Netherlands (responsible for any aspect of the collection, testing, processing, storage, release and/or distribution of human blood or blood components)
- Institution demographics
  - For blood establishments and blood services in 2019
  - Whole blood donations 413 653 and apheresis 313 811

**Question 2**

COVID-19 convalescent plasma (CCP) is solely being collected by plasmapheresis. There are no differences between CCP donors and routine plasmapheresis donors, meaning that in a consecutive period of 12 months, a donor is permitted to donate maximally 26 times, and collection is not allowed to exceed 25 litres of plasma (excluding anticoagulant). The donation volume is based on gender, height and body weight, but maximized to 750 ml of plasma excluding anticoagulant.

**Question 3**

In the Netherlands, CCP is collected for two reasons. In March 2020, we started with the collection of CCP. Mid of May 2020, also with the collection of source plasma for the production of COVID-19 was started. As of December 31, 2020 approximately 4500 collections for



CCP and 50 500 collections for SARS-CoV-2 immunoglobulins (COVIg) source plasma were performed. In the Netherlands, the fresh frozen plasma for transfusion is preferably used in clinical trials (e.g. the COV-EARLY trial, a study for pre-hospital infected patients, and the REMAP-CAP trial, a study for hospitalized infected patients) and for compassionate use in immune compromised hospitalized patients with persistent and/or severe COVID-19 disease.

#### Question 4

Starting with CCP collections in March 2020, in all donors COVID-19 infection needed to be proven by a positive SARS-CoV-2 PCR in the symptomatic period. (nose and/or throat swab). In June – August 2020, this eligibility criterion was not mandatory anymore for COVIg source plasma donors. However, since in source plasma donors only 60% had SARs-CoV-19 antibodies versus 85% in FFP donors, this criterion was re-introduced. The donor should be at least 14 days symptom-free from symptoms such as a cold, runny nose, sneezing, sore throat, coughing complaints, increased temperature and fever.

#### Question 5

No.

#### Question 6

No, not in general. Some of the donors are found positive in prevalence studies performed by Sanquin. These studies were performed with a SARS-CoV-2 total antibody ELISA (Wantai Biological Pharmacy Enterprise Co., Ltd., Beijing, China) [1].

#### Question 7

Starting July 2020, all CCP donations are routinely tested for SARS-CoV-2 IgG antibodies with a sensitive total Ab bridging assays for detection of SARS-CoV-2 Abs to the receptor-binding domain (RBD) and nucleocapsid protein in ELISA format. By using a cut-off value of 0.1 nOD, it is anticipated to provide ~99% specificity [2].

Prior to July 2020, two samples of 5 ml of EDTA whole blood were collected during donation together with samples for blood type and tests for transfusion transmissible infections from the diversion pouch of the apheresis disposable. After centrifuging of the EDTA tubes, the plasma was aliquoted and archived frozen at lower temperatures of  $-20^{\circ}\text{C}$  until routine anti-SARS-CoV-2 testing was started.

#### Question 8

In the Netherlands, the majority of the plasma for transfusion is pooled, solvent-detergent (SD)-treated, prion reduced plasma (Octapharma GmbH, Germany). A minority of the plasma is quarantined. Since there wasn't sufficient plasma collected for pooled SD treatment, no validated single donation SD treatment methods and no time for quarantining, no pathogen reduction to CCP for transfusion is applied which is according to the recommendations of ECDC [3].

#### Question 9

In the Netherlands, all donors who received one or more blood components since January 1980 are deferred permanently. Therefore, recipients of CCP are not accepted as donors.

#### Question 10

Similar to other infectious diseases, individuals recovered from COVID-19 are accepted as donors, irrespective of whole blood or apheresis, with a minimal interval of 14 days after recovery.

#### Question 11

As answered in question 9, in the Netherlands, all donors who received one or more blood components since January 1980 are deferred permanently. Therefore, recipients of CCP are not accepted as donors.

#### Question 12

One of the first challenges was recruitment of sufficient donors without having sufficient knowledge of the virus and test capacity for SARS-CoV-2 antibodies. Media platforms as social media, messaging applications, national papers, news programs, and radio/TV were initially largely overwhelmed by the notification of recently recovered COVID-19 patients. This led to a completely full reservoir of potential donors, resulting in long waiting lists for the first medical examination and donation. Unfortunately, despite major effort, only relatively low percentages of the registered persons could be accepted as donors because of medical or other reasons. We found out that the highest success rate to recruit CCP donors was by requesting physicians, hospitals, laboratories, and public health departments to inform recently recovered COVID-19 patients to become CCP donors.

Because our staff at the donor centres occasionally expressed concern on the potentially infectious status of “recovered patients” a thorough information of all staff was needed.

Another challenge was the need for additional spacing between collection beds. Social distancing of 1.5 metres reduced the collection capacity for approximately 40%. As a result, there was an additional competition with collecting of whole blood and especially source plasma since the same apheresis equipment was applied.

Challenging was also to work together with academic hospitals to draw up a study protocol for the use of CCP for COVID-19 infected patients in an amazing short time period. Since Sanquin Blood Supply is the only blood establishment in the Netherlands and thus the only legal provider of CCP, it was essential to become part of the study group. We also felt that the best way to issue CCP was for its use in clinical trials when evidence on the efficacy is still lacking. This resulted in the first randomized controlled study, which started recruiting patients in April 2020 [4].

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### Italy

Vincenzo De Angelis, Pierluigi Berti, Angelo Ostuni & Giuseppe Marano

### Question 1

The Italian National Blood Centre is the Italian blood and blood component competent authority operating under the aegis of the Ministry of Health. It coordinates and supervises the 21 Regional Coordinating Blood Transfusion Centres, with the aim of guaranteeing homogeneous standards of quality and safety throughout the blood system. Standards for CCP have been defined by the Italian National Blood Centre in a recent note of guidance (October 2020) [1]. In 2019, a total 2 996 264 collection procedures (whole blood and apheresis procedures) have been carried out in Italy.

### Question 2

In the initial phase of the emergency related to the COVID-19, the national policy adopted has included only the donation of plasma in apheresis from convalescent former patients. The latter may donate more than once according to the frequency for routine plasma donations by apheresis and depending on the criteria stated by law in order to protect the donors' health. At a later stage, the possibility of also collecting whole blood from donors with anti-SARS-CoV-2 antibodies was introduced. The donors (many of them are probably already regular blood donors) may donate more than once according to the frequency for routine whole blood or plasma donation by apheresis stated by the law in force [2]. Each unit of collected CCP must be clearly labelled as “Plasma unit collected from a convalescent patient-donor with a virologically documented diagnosis of COVID-19” and must report the titre of the neutralizing antibodies.

### Question 3

In Italy, the CCP, which is obtained from a convalescent COVID-19 donor, is intended only for transfusion and fractionation purposes. Although the Italian National Blood Centre recommended the use of CCP in clinical trials, possibly randomized, it has been transfused in emergency/compassionate situations. The Italian National Blood Centre is in charge of a regular monitoring of the CCP collection and transfusion. Up-to-now, a prevalent utilization in clinical trials has been detected.

### Question 4

Donors shall be eligible according to selection criteria stated by national law. Careful clinical evaluation is recommended with the focus on the apheresis criteria to protect the health of donor. Only male donors or nulliparous

females with a negative history of blood component transfusion are eligible to CCP for transfusion use; the others, can donate to fractionation purposes. Donors shall have a virologically documented diagnosis of COVID-19 based on a positive SARS-CoV-2 molecular swab healing test. Donors shall be completely recovered from the symptoms of COVID-19 and result negative in one SARS-CoV-2 molecular swab healing test. Plasma collection (donation) can occur 28 days after the negative nasopharyngeal swab in case of previous hospitalization; in other cases, at least 10 days after the onset of symptoms with a negative molecular test performed after at least 3 days without symptoms (only for symptomatic patients).

#### Question 5

No blood/serum SARS-CoV-2 molecular tests are required. To assess viral clearance, CCP donors must have a documented negative molecular swab healing test performed by laboratories competent for COVID-19 testing.

#### Question 6

The national policy states that the preliminary selection of CCP donors is based on a clinical history of disease evidence of recovery confirmed by a documented molecular swab healing test. Serological test for anti-SARS-CoV-2 antibodies can be performed either before or after donation. In Italy, several serological methods are currently available, each of them with a cut-off provided by the manufacturer. No serological cut-off criteria are still applied for accepting the donor for donation.

#### Question 7

The presence of anti-SARS-CoV-2 neutralizing antibodies shall be documented on donor/donation at the time of collection of CCP units intended for transfusion purposes (clinical trials). The national policy recommended to apply the cut-off defined in the specific clinical trials (e.g. the national "TSUNAMI study" - *Transfusion of convalescent plasma for the early treatment of pneumonia due to SARS-CoV-2*-requested CCP units with titre of at least 1:160), as well as to collect and store CCP unit samples for future assessment.

#### Question 8

The application of a pathogen inactivation method of recognized efficacy on SARS-CoV-2 was recommended as an additional safety measure in the national "TSUNAMI Study" (*Transfusion of convalescent plasma for the early treatment of pneumonia due to SARS-CoV-2*) and, in

general, for the clinical use of CCP in COVID-19 patients. The thawed and inactivated CCP can be stored at 4°C for up to 5 days [1].

#### Question 9

In order to prevent the Transfusion-Related Acute Lung Injury (TRALI), donors with a history of blood component transfusion, including CCP transfusion, are not eligible to donate CCP for clinical use. Plasma from recipients of CCP may be collected for fractionation purposes.

#### Question 10

Individuals are eligible for standard whole blood or apheresis (platelet or plasma) donation if they are completely recovered from COVID-19 infection and tested negative for SARS-CoV-2 molecular swab healing test. The potential donors must be compliant to the selection criteria stated by law in force [2]. The minimum deferral period after recovery before whole blood or apheresis donation is 10 days.

#### Question 11

According to the selection criteria stated by law in force [2], recipients of CCP are eligible for standard whole blood or apheresis donation. In order to prevent the Transfusion-Related Acute Lung Injury (TRALI), donors with a history of blood component transfusion, including CCP transfusion, are eligible to donate plasma only for fractionation purposes.

#### Question 12

The SARS-CoV-2 stressed our capacity to respond to an infectious disease outbreak. The need to equip ourselves with standardized and homogeneous risk assessment tools at national and international level has become increasingly evident so to increase the necessity to build-up blood components collection programmes in emergency situations and from former patients (convalescent subjects).

In addition, more evidence from high quality clinical trials is required to fully demonstrate the efficacy of CCP therapy and to design a single protocol that defines the product specifications in terms of quality, neutralizing antibody titre and therapeutic indications.

Among those on the market, it is also advisable to identify a serological test for the detection of neutralizing antibodies, which correlates with the results obtained by means of *in vitro* neutralization tests.

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## Belgium

Michel Toungouz Nevessignsky

### Question 1

- Type of institution
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- Institution demographics
  - For blood establishments and blood services
    - Approximate number of whole blood and apheresis collections made/year for RBCs, platelets and plasma (as applicable):
    - 160-000 RBC, 11-000 PLT, 25-000 Plasmas collections/year

### Question 2

Same as usual plasma donation: 23/year (15 litres/year, 2 litres/month taking into account 650 ml per plasmapheresis) with the limitation of a defined titre of neutralizing anti-SARS-CoV-2 antibodies.

No.

### Question 3

Both.

### Question 4

Yes, both.  
Absence of symptoms.

### Question 5

No.

### Question 6

No. The test is performed at the time of donation and a defined titre of neutralizing antibodies is used as a release criteria.

### Question 7

No.  
Yes.

### Question 8

Yes.  
Yes, methylene blue.

### Question 9

Theoretically yes with a temporary exclusion of 4 months.

### Question 10

Yes.  
28 days

### Question 11

Yes.

### Question 12

Donor recruitment, performing the neutralization assay and getting the results on time, convincing the collecting staff to welcome convalescent donors, managing physician pressure related to compassionate use and being able to provide enough plasma units for the studies.

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## Egypt

Magdy El Ekiaby

### Question 1

- Type of institution

*Hospital-based blood services* (a hospital unit performing the functions of blood establishment and transfusion services at a hospital level)

- Institution demographics
  - For hospital
    - Number of in-patient beds 100
    - Approximate number of RBCs transfused/year 25 000
    - Age group of patients treated (neonates, paediatrics <18 years, adults >18 years) All ages
    - Type of patients treated (medical or surgical) Both

### COVID-19 donor pre-selection criteria

- Physical examination of the donor to establish health status and suitability for plasma donation according to Egypt donor selection criteria (lower haemoglobin level down to 11 gm/dl for males and 10.5 gm/dl for females might be allowed)
- Confirmation of previous infection with SARS-CoV-2 by previous positive PCR swab
- Confirmation of the resolution of the infection through demonstration of two repetitively (at least 24 h interval) non-reactive PCR swab or 10 days after disappearance of symptoms
- Male donors or nulliparous female donors
- Selected donor should test positive to SARS-CoV-2 antibodies (IgG or combined IgM and IgG antibodies)
- Approximative date of COVID-19 infection, symptoms and treatment received should be documented and traceable

Plasma collection:

### Question 2

Once every 2 weeks. In practice, donors were not regular donors so they donated only one or two times.  
 Not different.

We did not collect whole blood.

### Question 3

Trial use.

### Question 4

Yes. Anti-SARS-CoV-2 antibodies.  
 Disappearance of symptoms for 10 days or more + presence of anti-SARS-CoV-2 antibodies.

### Question 5

No.

### Question 6

Yes using anti-SARS-CoV-2 rapid test from AMEDA Labor Diagnostika, Austria.

### Question 7

Anti-SARS-CoV-2 antibody test IgM & IgG using Maglumi Chemiluminescence assay from Sibe China (cut-off 1) and Chemiluminescence assay on Centaur from Roche.  
 Yes for neutralizing antibody assay.

### Question 8

We are processing Convalescent COVID-19 plasma into anti-SARS-CoV-2 hyperimmunoglobulin, which includes lipid enveloped virus inactivation step by Caprylic Acid.

### Question 9

Only within a clinical study.

### Question 10

We do not have a specific question about COVID-19 previous infection during medical screening for regular blood or apheresis donation.  
 If donor states that he/she had recent COVID-19 infection we temporary defer.

### Question 11

So far there is no policy.

### Question 12

National standards are still not set.

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## Australia

James Daly and Veronica Hoad

### Question 1

- Type of institution
  - National Blood Services/Blood Centre (responsible for recruiting donors; screening and selecting blood donors; blood collection; testing and processing blood units; transporting; receiving and storage of blood units; pre-transfusion testing, and issuing blood for clinical transfusion at a national level)
  - Also supply plasma for fractionation to fractionator
- Institution demographics
  - Approximate number of whole blood and apheresis collections made/year for RBCs, platelets and plasma (as applicable):
  - 2019/2020 financial year collections 1 527 089
  - Collections: Whole blood 690 115, plasmapheresis 809 910, Platelets 27 024
  - Components: Red cells 630 993, clinical plasma 238 541 platelets (pooled and apheresis) 138 629 and plasma for fractionation 802 630 kg

### Question 2

COVID-19 Convalescent plasma donors may donate by plasmapheresis as frequently as weekly for up to 12 donations. This is more frequent than standard plasmapheresis donations but the same maximum limit for a 12 month period is applied which is up to 33 per year.

We introduced additional monitoring for total protein and Immunoglobulin levels for frequent donors.

Yes, donors are encouraged to make apheresis plasma donations but Whole blood donations are accepted. Because donors are required to meet all other donor eligibility criteria and the collection and processing of the donation is the same as standard donations, the red cells from the whole blood donation are labelled as standard red cells and the platelets may be pooled as standard platelets.

### Question 3

Convalescent plasma donations from male donors with a neutralizing antibody titre at or greater than 1:80 are

suitable to be used for transfusion in clinical trials. This was used for clinical trials for symptomatic COVID-19 infection in hospitalized patients (ASCOT trial) and patients admitted to Intensive care (REMAP-CAP).

Convalescent plasma donations with a neutralizing antibody titre at or greater than 1:40 were suitable for fractionation to manufacture of COVID-19 immunoglobulin. This product has not yet been used in clinical trials.

COVID-19 Convalescent plasma was approved to be issued for use in clinical trials (ASCOT and REMAP-CAP trials). The initial intention was not to support compassionate use because there was insufficient evidence of benefit from convalescent plasma. Only 2 requests for compassionate access to COVID-19 convalescent plasma were approved – both were for immunosuppressed patients unable to mount an antibody response and with prolonged COVID symptoms/PCR positivity.

### Question 4

No. Donors must report that they had 'laboratory confirmed COVID-19 infection' as per our National guidelines for a confirmed case. A copy of the diagnostic report was not required to be provided.

The vast majority were positive by RNA but the confirmed case definition also includes seroconversion and a rise in IgG. For reference the current case definition is:

- (i) tested positive to a validated specific SARS-CoV-2 nucleic acid test, or
- (ii) had the virus isolated in cell culture, with PCR confirmation using a validated method, or
- (iii) undergone a seroconversion to or has a significant rise in SARS-CoV-2 neutralizing or IgG antibody level (e.g. four-fold or greater rise in titre).

Note: Serological confirmation was added to the national case definition on 13 May 2020, so this only applies to donors who have had their diagnosis confirmed by serology after this date. For the diagnosis to be confirmed by this method usually this requires additional evidence to undergo the testing, such as symptoms consistent with COVID-19 where they have tested negative on PCR or an epidemiological link to a confirmed case.

COVID-19 convalescent plasma donors had to have laboratory confirmed COVID-19, and be at least 28 days from recovery of symptoms, and meet all other standard donor eligibility criteria. Minor residual symptoms are allowed after Medical Officer Assessment (e.g. some residual loss of smell).

Only male donors were eligible for clinical plasma donation (as per existing TRALI risk reduction measures for plasma donors).

Donations with a Neutralizing antibody titre greater or equal to 1:80 were suitable for clinical plasma.

Donations with a Neutralizing antibody titre greater or equal to 1:40 were suitable for manufacture of COVID-19 immunoglobulin.

#### Question 5

No.

#### Question 6

No, this is done at the time of donation for every donation to determine if the donation is suitable for release as a convalescent plasma product as described below.

#### Question 7

Each donation is tested by a reference laboratory using 3 separate tests, the Abbott Architect SARS-CoV-2 IgG CMIA, the Euroimmun anti-SARS-CoV-2 ELISA and a virus microneutralization assay using Vero E6 cells. The results were reported as per the product inserts. The microneutralization description can be found here: <https://www.medrxiv.org/content/10.1101/2020.12.07.20245696v1>

Evaluation of the assays determined that low-level neutralization antibody positive donations would be missed if the donation did not progress to the neutralization antibody test if testing was ceased with a negative or equivocal screening antibody test. The neutralization assay was considered the definitive release test.

However, for a donation to be considered suitable for clinical convalescent plasma the donation must test positive on one of the two screening tests and have a Neutralizing antibody titre greater or equal to 1:80.

For a donation to be suitable for COVID-19 Immunoglobulin production the donation required a neutralizing antibody titre greater or equal to 1:40 as the sole test.

Yes, we collected 4 tubes and 2 were used for preliminary testing with an additional 2 tubes saved for further testing/research purposes.

#### Question 8

No. No clinical plasma in Australia has additional pathogen reduction.

#### Question 9

No. Transfusion of blood products is an existing exclusion criterion for blood donors (for 12 months since the transfusion). All Convalescent plasma donors must meet all existing donor eligibility criteria.

We have not had significant usage of convalescent plasma in the clinical trials and therefore there are no issues with this policy, which is longstanding. However, there is no regulatory requirement for this deferral so if we were in the situation of other countries where many patients had received convalescent plasma and there was a sufficiency issue, we would reconsider.

#### Question 10

Yes, donors are eligible for standard blood component donations if they are at least 28 days from recovery of symptomatic COVID-19 and meet all other donor eligibility criteria. Donors that have had laboratory confirmed COVID-19 would be encouraged to make a convalescent plasma donation by apheresis. Those donations that do not meet the minimum 1:40 neutralizing antibody titre are used as standard donations.

#### Question 11

No. Transfusion of blood products is an existing exclusion criterion for blood donors (for 12 months since the transfusion). All Convalescent plasma donors must meet all existing donor eligibility criteria.

#### Question 12

Government approval was required before we could commence collections and therefore important to engage and continue the dialogue early as the procedures take time to set up and in the end it was difficult to manage a large program in a small timeframe.

Set up before any evidence on possible effectiveness or before fractionators determined what would likely be a standard level of neutralizing antibody required. It is difficult to change cut-off criteria without definitive evidence on effectiveness but retrospectively would have used higher cut-off for acceptable titre.

Despite having a reasonable sized second wave as we are the collectors and not the users we were reliant on the clinicians and trial coordinators in the hospitals to assess and consent patients for convalescent plasma in the trial environment. Many patients were not suitable and to some degree there was not optimal usage when patients were in hospital during the second wave, which was successfully suppressed that limited further enrolment.

Very grateful that we used exactly the same criteria for existing donation so our donations will not go to waste if CP is determined to be ineffective or only high titre units are acceptable, as they can be used as regular FFP or for plasma for fractionation. That is an important message and outcome to all CP donors who have donated. Their

donations will still be used to help patients in need, no matter what.

### *Extra information about CP donations*

As at January 11th 2021 we have 809 convalescent plasma donors with 3160 collections. Of all donations tested only 5.9% of donations were negative, 40.7% were low-level positive (1:40) and 53.4% were positive with a level  $\geq 1:80$ . We used 46 clinical plasma units in clinical trials and for compassionate use and have 480 in stock with an inventory aim of 500. We have sent 1377 kg of fractionated plasma to CSL Behring.

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## **South Korea**

Sinyoung Kim

### *Question 1*

- Type of institution;
  - Hospital-based Blood Transfusion Service/Blood Bank
- Institution demographics
  - Tertiary referral hospital
    - 2437 in-patient beds
    - 50 200 RBCs transfused/year
    - All age group of patients treated
    - All type of patients treated

### *Question 2*

Plasmapheresis only

CCP donations are allowed every 2 weeks. This cycle is the same as routine plasma donation in South Korea.

### *Question 3*

CCP is collected for transfusion, especially for COVID-19 patients participating in clinical trial.

### *Question 4*

CCP collection is possible for donors 14 days after quarantine release. However, confirmatory PCR testing should

be performed for donors between 14 and 28 days of quarantine release.

Confirmed patients can be released from quarantine if they do not show any symptoms for 10 days upon confirmation, or test negative on PCR test twice in a row with at least a 24-h interval.

### *Question 5*

No.

### *Question 6*

No.

### *Question 7*

Yes. Every CCP unit was tested for anti-SARS-CoV-2 antibodies using AFIAS COVID-19 IgG Ab (Boditech Med., Korea). CCP unit showing positive COVID-19 IgG Ab result (cut-off index  $>1.0$ ) can be supplied for transfusion.

Samples from the CCP unit have been stored for future study.

### *Question 8*

Pathogen inactivation technique is not available in South Korea.

### *Question 9*

No.

### *Question 10*

Yes, the deferral period is 3 months for blood donation.

### *Question 11*

Yes. Recipient of blood and blood products is deferred for 12 months following transfusion including CCP.

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## **South Africa**

Karin van den Berg, Marion Vermeulen & Tanya Nadia Glatt



**Question 1**

Regional Blood Service  
 Whole blood collections per annum: 900 000  
 Apheresis platelet collections per annum: 18 138  
 Apheresis source plasma collections: 32 000  
 RBC issued per annum: 810 000  
 Pooled platelet issued per annum: 33 000  
 Apheresis platelets issued per annum: 32 000  
 Fresh frozen plasma issued per annum: 123 000

**Question 2**

To date, SANBS has been collecting CCP through plasma-pheresis. Donors are allowed to donate once every 2 weeks with a maximum of 24 procedures per annum. This donation frequency is the same as the source plasma program.

Our CCP program is based on the recently implemented source plasma program. This enabled us to rapidly develop and implement a CCP collection program with a near-national footprint. SANBS have source plasma collection equipment and trained staff in most of the major cities and towns in South Africa. Piggy-backing on this program significantly decreased the set-up time we would otherwise have needed.

We recently started a SARS-CoV-2 seroprevalence study among our blood donors. The unexpectedly high prevalence of SARS-CoV-2 antibodies have raised the potential for us to use whole blood recovered plasma for CCP, but this process is not yet fully developed. However, this would certainly be a consideration for other LMIC blood services.

**Question 3**

Currently, we have two programs for which we are collecting CCP. Firstly, we are collecting high titre CCP for a double blind randomized phase III clinical trial assessing the efficacy of CCP in the treatment of hospitalized patients with moderate to severe COVID-19. Secondly, we are collecting CCP (regardless of titre) for our national fractionator, the National Bioproducts Institute, who is participating in the CoVIg-19 program and preparing a test, not-for-human-use batch of SARS-CoV-2 immunoglobulin.

In addition, we recently started a directed CCP program, which enables clinicians to arrange for the collection of CCP from donors they have identified and to which the patient has agreed. This is a compassionate use type program where SANBS's role is limited to the collection of the plasma.

**Question 4**

All CCP donors (who donate for the clinical trial or the fractionation program) must have a confirm test result of past COVID-19 infection prior to being accepted as CCP donors. We accept either a SARS-CoV-2 RT-PCR or Ag test or the presence of SARS-CoV-2 antibodies.

Eligibility criteria for our CCP donors include [1]:

At least 28 days since last symptoms OR 14 days since test, with 2 negative results at least 24 h apart. This was subsequently amended to 14 days post last symptoms

Must be between the ages of 18 and 65

Males and nulliparous females only

Must meet general blood donor criteria

**Question 5**

No, we do not test prospective CCP donors for SARS-CoV-2 prior to accepting them for donation.

We request a copy of their SARS-CoV-2 test and confirm that they meet the "recovery" criteria as mentioned above.

**Question 6**

Currently, donors donating for the clinical trial and fractionation programs undergo a "pre-test" prior to their first donation. This pre-test includes the full set of routine donation screening tests (HIV, Hepatitis B and C as well as Syphilis) as well as SARS-CoV-2 ELISA antibody test. Initially all donors with detectable SARS-CoV-2 antibodies were accepted, but following publications suggesting that efficacy of CCP may be influenced by antibody titres [2], we only accepted donors with a set cut-off for further donations.

(The National Institute of Communicable Diseases perform the antibody ELISA using a method based on the test developed by Kramer and colleagues [3]. An arbitrary cut-off for a positive was an optical density (OD) of 0.4. However this was later increased to 1.0 for inclusion into the CCP program.

**Question 7**

Yes, all CCP units collected at SANBS are tested for anti-SARS-CoV-2 antibodies. Donors are tested before they donate their first unit and then at each subsequent donation. Currently, the antibody testing is performed by the South African National Institute of Communicable Diseases. Samples are first tested using an ELISA test and then those with a sufficiently high OD are tested for neutralizing antibodies. Recently however, following

publications suggesting that ELISA tests are likely sufficient to identify high titre plasma [4], we have decided to discontinue the neutralizing antibody testing.

Yes, we are collecting samples from the CCP units for future research purposes. These samples are frozen and archived. Use of these samples for projects other than the current projects is at the discretion of the PI of our CCP donor program.

#### Question 8

Products intended for the clinical trial (therefore for human use) are pathogen reduced using the Cerus Intercept system.

Perhaps important to note that SANBS currently do not perform pathogen reduction on any of our routine blood products. The decision to implement pathogen reduction for these products is based on the fact that we employ a “donor retested quarantine” program for plasma products intended for patient use. This is part of our blood safety strategy in a country with the biggest HIV epidemic in the world. We were not able to set-up a quarantine program for the CCP donations. Considering the large volume plasma transfused and the high proportion first time donors among the CCP donors, we decided to implement pathogen reduction for the CCP program.

#### Question 9

SANBS currently have a 3-month deferral period for recipients of blood products. This would therefore apply for recipients of CCP. Other than this, we do not currently have specific exclusions for recipients of CCP. If they meet all the eligibility criteria, including having a sufficiently high SARS-CoV-2 antibody titre and have waited out their 3 month deferral period we would likely accept them. We have, to date, not been confronted with this situation.

#### Question 10

Yes, we do accept individuals recovered from COVID-19 infection for standard whole blood and apheresis donation as long as they have fully recovered and have been symptom-free for 14 days prior to presenting to donate.

#### Question 11

Yes, we do accept CCP recipients for routine blood donations, both whole blood and apheresis.

These donors are subject to the SANBS general deferral of 3 months following the receipt of blood or blood products.

#### Question 12

- Challenges:
  - South African legislation prohibits paid-plasma programs, which significantly hampered the rapid scale-up of this program.
  - SANBS has a limited footprint of trained staff and equipment for the collection of apheresis plasma. This, in combination with the high levels of poverty in the country meant that most COVID recovered patients were not able to donate plasma, as there were no apheresis units located near these sections of the population.
  - The lockdown levels in South Africa with the requirement for anyone who can to work from home to do so, significantly hampered our ability to recruit donors in traditional ways and places.
  - South Africa does not allow payment of blood donors, not even for plasma collections intended for fractionation. This further limited our ability to collect plasma and it meant that we would probably not be able to collect sufficient CCP for large-scale routine use.
  - During certain periods of the epidemic SANBS face severe blood shortages. The CCP program competed with the routine blood collections not only for donors but also for staff. SANBS staff was severely affected during the second wave of the epidemic in South Africa and we had to carefully assess the need for CCP collections versus whole blood collections.
  - Some SANBS staff at CCP collection sites were apprehensive to manage CCP donors for fear of them still being infectious. This required appropriate, ongoing education and training.
  - Some CCP donors were eager to donate but were concerned about the effect CCP donations would have on their own immunity to reinfection. This required appropriate education.
  - It was difficult to maintain CCP donations during the annual extended summer holiday when many donors went on holiday and missed at least one donation.
  - Routine SARS-CoV-2 antibody testing was not available for the first few months of our CCP collections. There were some donors who may have been using their CCP donation to get a SARS-CoV-2 antibody result instead of being completely altruistic.
  - Another challenge was the lower than expected frequency of high titre anti-SARS-CoV-2 antibody levels. This meant that more donors than were

expected were required to meet the clinical arm of the study and many operational procedures and system modifications were required to ensure lower titre plasma was not issued to patients.

- **Lessons Learned:**

- Early, ongoing collaboration is key. Locally, collaborations with clinicians and academics meant that we were responsive to the “real-world” needs and challenges faced by those caring for COVID-19 patients. Working side-by-side with our National Institute of Communicable Diseases (NICD) again enabled us to keep informed of new developments in the South African epidemic, but also provided the NICD with ready access to samples for ongoing research. Internationally, the collaboration with the ISBT Working Party has been invaluable. We learned so much from our international counterparts and were able to assess what others were doing and seeing what would work best for our local setting.
- Rapidly developing a new product program requires various internal stakeholders to work together in a seamless fashion all geared towards achieving a common goal. Ensuring early buy-in and excitement within the organization is key to achieving rapid change in an organization, which is generally quite change and risk averse.
- Correct marketing is key to ensuring an adequate CCP supply. Recovered COVID-19 patients are eager to donate CCP, even if they are not regular blood donors, when they realize the possible effect their CCP can have. Although we are not allowed to call potential CCP donors directly, an effective way to acquire donors is to ask clinicians to educate patients about CCP donation on discharge from hospital. Recovered patients trust their clinician and are likely to want to become donors. This enables us to get CCP donors who were hospitalized, and likely to have higher antibody titres. Ineligible donors, such as those too young or too old, would not be recruited by clinicians reducing the time required by our staff to manage these ineligible donors.

### Section References

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## Germany

Richard Schäfer

### Question 1

Type of institution.

- **Regional Blood Services/Blood Centre** (responsible for recruiting donors; screening and selecting blood donors; blood collection; testing and processing blood units; transporting; receiving and storage of blood units; pre-transfusion testing, and issuing blood for clinical transfusion at a regional level)

Institution demographics.

Whole blood donations: 5849/year.

Apheresis: platelets: 379; plasma: 23; RBCs: very rare (<5).

### Question 2

CCP is collected exclusively by plasmapheresis:

The allowed frequency is 60 plasma donations per year (same as routine plasma donation by apheresis) with a minimum of 2 calendar days between 2 donations.

Plasma from whole blood donations is not used for CCP.

*Question 3*

The collected CCP is intended for transfusion for both compassionate use and trial use.

*Question 4*

Yes.  
Both SARS-Cov-2 PCR, or anti-SARS-Cov-2 antibodies can be accepted.  
4 weeks without symptoms; no (long-term) sequelae

*Question 5*

Yes.  
The PCR sample is collected during the pre-donation visit (typically 14 days prior to donation). A donation is possible earliest 14 days after negative PCR testing.

*Question 6*

Yes.  
An in-house plaque reduction neutralization test (PRNT) is used to detect and quantify neutralizing antibodies; titres >1:20 are acceptable.

*Question 7*

Anti-SARS-CoV-2 antibodies are tested at each donation from donor blood samples (not the CCP unit).

*Question 8*

No.

*Question 9*

No.

*Question 10*

Currently, the minimum deferral period after recovery from COVID-19 is 4 weeks.

*Question 11*

Currently, the minimum deferral period after blood component transfusion is 12 months.

*Question 12*

The major challenge was having enough donors getting cleared for CCP donation because of substantial dropouts due to unacceptable medications, low Hb and positive testing for HLA antibodies.

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**United States – OneBlood**

Rita Reik, Richard Gammon & Melissa Lopez

*Question 1*

- Type of institution
  - **Regional Blood Services/Blood Centre** (responsible for recruiting donors; screening and selecting blood donors; blood collection; testing and processing blood units; transporting; receiving and storage of blood units; pre-transfusion testing, and issuing blood for clinical transfusion at a regional level)
- Institution demographics

Please see the table for calendar year 2020 data.

## Actuals- Current Year: 01/01/2020 to 12/31/2020

	Autologous	Allogeneic	Directed	Therapeutic	HH	TT	Total	s
2 units RBC		51 014	35				51 049	5.44%
Granulocytes			34				34	0.00%
Plasma Apheresis		10 434	2				10 436	1.12%
Platelet Apheresis		48 361	146				48 507	5.17%
Platelets and Concurrent Plasma		29 437	65				29 502	3.14%
RBC with Plasma		4641	3				4644	0.49%
RBC with Platelets		280	3				283	0.03%
RBC with Platelets and Plasma		839	8				847	0.09%
Single Unit Recovery		2696	2				2698	0.29%
Stem Cells			13				13	0.00%
Whole Blood	362	750 423	1215	14,697	6329	17 674	790 700	84.23%
<b>Total</b>	<b>362</b>	<b>393 175</b>	<b>1526</b>	<b>14 697</b>	<b>6329</b>	<b>17 674</b>	<b>938 763</b>	<b>100.00%</b>
%	0.04%	95.68%	0.16%	1.57%	0.67%	1.88%	100.00%	

*Question 2*

Donation frequency is generally a minimum of 28 days or the same as standard plasmapheresis donation. The US Food and Drug Administration (FDA) considers these to be infrequent plasma donors and allows an exemption from additional history, physical and testing requirements of those who donate more frequently [1]. Contingent upon need, a reduced deferral period can be determined at the Medical Director's discretion, and depends on the type of donation, and specific donor characteristics, donation history and urgency of the situation.

When the Medical Director uses his or her discretion, this differs from the donation frequency permitted for routine plasma donation.

Yes. The rationale is based upon the fact that these products are derived from persons who have met all the usual blood donor eligibility criteria [2,3] and testing for relevant transfusion-transmitted infections [4] must be performed and the donation must be found suitable [5]. In fact, at OneBlood, CCP may be prepared from all qualified traditional blood donors who test positive for SARS-CoV-2 antibodies using orthogonal testing to confirm naturally-acquired immunity. Red blood cells and platelets are labelled as per standard operating procedure in these instances.

*Question 3*

CCP is collected for compassionate use as well as clinical trial use. CCP is not currently collected at OneBlood for fractionation purposes. The CCP collected is primarily

intended to be used immediately to meet patient needs, however, effective efforts have been made to build a stockpile of CCP inventory for future use and as a backup plasma supply as needed.

*Question 4*

The criteria have evolved over time. Initially the donors were required to have proof of infection in the form of a positive polymerase chain reaction (PCR) test and/or antibody test, 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 [6]. Currently there are two sources of CCP: (1) volunteer CCP donors with a history of COVID-19 who are now symptom-free and (2) traditional blood donors with an unknown history, who upon testing their donation sample, are found to have antibodies to both Spike and Nucleocapsid proteins ("orthogonal" testing). At present, the BC requires the CCP donors to be symptom-free for 14 days and test positive for both Spike and Nucleocapsid antibodies at the time of donation. Individuals who have received the SARS-CoV-2 vaccine may donate CCP if they had symptoms of COVID-19 and a positive test result from a diagnostic test approved, cleared, or authorized by FDA, and received the COVID-19 vaccine after diagnosis of COVID-19, and are within 6 months after complete resolution of COVID-19 symptoms [6].

Recovery is defined as the absence of symptoms such as cough, fever, body aches, neurologic or other unusual symptoms for at least 14 days for those donors with a history of COVID-19.

*Question 5*

No.

*Question 6*

Both CCP and traditional donors' blood samples are collected at the time of donation and tested for SARS-CoV-2 antibodies. (Cut-off criteria listed in question 7).

*Question 7*

Two test methodologies are used. The screening assay is the Ortho VITROS<sup>®</sup> SARS-CoV-2 Total (detects anti-Spike protein). If the signal-to-cut-off (S/C) ratio is 10 or greater, then this result is confirmed by the Roche Elecsys anti-SARS-CoV-2 assay (detects anti-Nucleocapsid protein). (Note: Per the manufacturer a S/C ratio of one is considered positive on the Ortho test but at OneBlood we use a higher S/C ratio to qualify a unit for CCP. The rationale is that correlation testing has confirmed that a higher S/C ratio corresponds to higher titres of SARS-CoV-2 antibody levels). If both test results are positive, then the unit qualifies for the manufacturing of CCP. The US Food and Drug Administration (FDA) will be requiring plasma donations to be tested by the Ortho VITROS SARS-CoV-2 IgG test and found to have a signal-to-cut-off (S/C) ratio of 12 or greater to qualify as a High Titre CCP, effective on 1 June 2021 [6,7].

Both serum and plasma samples are collected if needed for future assessment.

*Question 8*

No.

*Question 9*

Yes.

*Question 10*

OneBlood follows the US FDA requirements for deferral of CCP, which is complete resolution of symptoms at least 14 days before the donation [6]. This is for the safety of the donor collection staff.

*Question 11*

There is a three-month deferral required by the US FDA. This is consistent with the deferral required for transfusion recipients of Whole Blood or blood components such as packed red blood cells, platelets or plasma [8].

*Question 12*

In reflecting on lessons learned and challenges throughout the process, the following key areas were identified [9]:

*1. Data*

Comprehensive data was lacking regarding the regional and national blood supply, the number of units available in hospitals, and hospital usage patterns. This impaired the ability of the BC to predict the effect of the pandemic on the blood supply. As it impacted a large portion of the nation's BCs simultaneously, it affected the BCs ability to move blood from unimpacted to impacted areas. Additionally, lack of data impaired the BCs ability to predict the effect of cancellation of elective procedures or the regional need for blood products, a capability that would have proven invaluable for integrating CCP production planning into operations.

*2. Communication and Coordination*

There were issues with communication at all levels, particularly nationally; highlighting the need for enhancing existing networks and communications pathways and keeping them open. Various parts of the nation were impacted in different ways and times by the pandemic, resulting in disjointed communications between regions and national organizations regarding prioritization of need for resources. The FDA and other national and regional organizations compensated for these gaps by making themselves available at all times. At the regional level, the BC Communication team's proactive approach proved effective in controlling messaging to employees and the public.

*3. Donor recruitment*

CCP donor recruitment challenges were mainly attributable to the BC lack of access to qualified CCP donor lists. This resulted from regulations intended to protect patient privacy but had the unintended consequence of inhibiting the hospitals and health departments from sharing needed information about individuals who had recovered. This resulted in weeks of delay in CCP inventory development. Another donor recruitment lesson learned was related to timing. Initially, FDA required a 28-day deferral period after a CCP patient became asymptomatic. Since the epidemic was in its early stages in the US, many COVID-19 convalescent individuals had only recently recovered from their illness. Therefore, the 28-day wait period significantly limited the size of the eligible donor base. Another ongoing donor-related challenge was inconsistent national messaging regarding disease risk and mitigation.

#### 4. Testing

The lack of licensed tests for SARS-CoV-2 presented challenges to donor recruitment and CCP product characterization. There was a plethora of new serologic and molecular tests on the market for SARS-CoV-2 that had received emergency use authorization (EUA) by FDA, however lack of test availability remained an issue throughout the two phases. Trained staff were required to check the FDA website of EUA approved tests to determine if the test qualified [10]. This process was an impediment to rapid donor intake and processing. Since there were no widely available antibody titre tests to verify CCP product efficacy the FDA recommended additional donor samples were to be collected and stored for future titre testing. The availability of extra sample tubes proved critical for later titre testing and research.

#### 5. Personal Protective Equipment (PPE) and other supplies

The need for additional PPE put a strain on the BC at a time when there were national shortages. Severe supply chain shortages of PPE, disinfectants, paper goods and apheresis kits persisted throughout the project. This created pressure on BC administration to find needed supplies, an effort that was hampered by lack of prior relationships with vendors. Single source suppliers and just-in-time inventory practices, initially designed to reduce BC expenditures, exacerbated the situation.

#### 6. Messaging

Inconsistent national messaging regarding risk, safety of blood donation and need for PPE resulted in ongoing confusion of donors and staff as to what social distancing measures were appropriate and resulted in the loss of significant numbers of donors and drive cancellations. Proactive communication strategies using social media, emails and traditional media helped to maintain open lines of dialogue with employees and the public, who were reassured by consistent messaging that the BC followed all recommended FDA and Centers for Disease Control and Prevention (CDC) guidelines for protective measures and that it was safe to donate.

#### 7. Hospitals and Clinicians

Clinicians were unfamiliar with CCP resulting in hospitals and physicians being inadequately prepared for the rollout of the product. 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 availability and use of the product. This required ongoing communication between clinicians and BC

physicians. Convalescent plasma had been used in previous viral outbreaks for decades, yet only in March of 2020 did FDA authorize it for BCs to collect and physicians to use under an emergency investigational new drug (eIND) or expanded access program (EAP) for treatment of COVID-19. The EAP and eIND pathways were unfamiliar to some non-research-based hospitals and BCs, which found the requirements cumbersome. The lack of coordination and preparation at the BC/hospital level with the national programs (eIND and EAP) and the need for use of manual systems during the early development of the program caused delays and frustration. Physician and public lack of education regarding the challenges faced in implementing a CCP program led to public relations issues for the BC, which was expected to be able to produce CCP on demand, like other blood products.

Another lesson learned was that while a CCP donor may present, there is no guarantee that a successful collection will occur. Even if CCP is obtained, ABO incompatibility might make the unit unsuitable. This was also a point of education for the ordering physicians who recruited family members to provide directed donations. Situations occurred in which family members were assured that the unit would be obtainable shortly after the donation only to discover later that the unit was unusable for various quality reasons.

#### 8. BC Supporting Infrastructure

The pre-existence of a strong implementation support structure including the Project Management Office (PMO), in-house Information Technology (IT)/Business Intelligence (BI) and Business Continuity Plan (BCP) teams prior to the onset of the pandemic greatly enhanced BC responsiveness to the CCP project challenges and proved to be critical in disaster management. The PMO at the BC consisted of a dedicated, experienced team of professionals who were rapidly deployed on the project to develop and revise processes and training in response to frequent changes in FDA requirements. This department played a pivotal role in ensuring the success of the project. IT/BI was instrumental in streamlining and automating the intake and distribution aspects of the process. The BI team tracked and transformed complex data into highly functional dashboards and reports that allowed real time assessment and strategy development.

The BCP team performed daily horizon scanning on a global level and kept BC Leadership apprised of the progression of the pandemic and any additional threats. They gathered the CCP implementation team together daily for updates to facilitate and maintain communication in an extremely fluid environment.

### Section References

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### United Kingdom

Lise Estcourt, Sheila MacLennan & David Roberts

#### Question 1

NHS Blood and Transplant (NHSBT) is a national blood establishment that provides blood components for all hospitals in England. Until March 2020 NHSBT did not have a plasmapheresis service, this has been set up to provide convalescent plasma to the two trials that are being conducted in the UK (RECOVERY and REMAP-CAP). During 2019 we issued 1.4 million RBCs, 255 000 platelet units and 260 000 plasma units. Only platelet components were collected by both apheresis and whole blood donations

during 2019. In 2020 we have established a plasmapheresis service for convalescent plasma and have collected over 30 000 units of plasma.

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

##### Question 2

Convalescent plasma is collected via plasmapheresis. Donors can donate up to every week up to a maximum of 24 times annually. A donor can donate plasma as long as their antibody levels remain at high or medium levels (Euroimmun  $\geq 3$ ), however we test total protein levels after every 8 donations to ensure protein levels remain normal. Some of our donors have donated up to 20 times. We do not have a standard plasmapheresis service for collection of plasma other than convalescent plasma at the present time.

##### Question 3

CCP is collected for transfusion. We are using CCP within two trials RECOVERY (<https://www.recoverytrial.net/>) and REMAP-CAP (<https://www.remapcap.org/>). A few units have been issued outside of the trial for patients who are ineligible for either trial. Data on these patients will be collected as part of the CLEARANCE registry. We are not fractionating plasma, any change to this policy will require UK government authorization.

##### Question 4

Donors for CCP donation have to meet our standard blood donor criteria. The only exception to this is that previous CCP recipients can become CCP donors but they cannot become standard whole blood or platelet apheresis donors. Potential female donors also have to have negative HLA and HNA antibody tests.

Donors may donate 28 days after recovery. Our definition of recovery from SARS-CoV-2 infection is when the donor is generally well and back to normal activities and no longer has significant fatigue which affects daily activities, fever, respiratory symptoms, cardiac or other symptoms such as headaches or dizziness.

##### Question 5

No. We do not require donors to be tested for SARS-CoV-2 by PCR before donation. However, we do insist it has to be at least 28 days since recovery from their symptoms prior to donating plasma.

##### Question 6

We do not test antibodies levels prior to donation for men who have had a previous positive PCR test for



anti-SARS-CoV-2 prior to donation. This is because we have found that 25% of these donors will have high antibody levels (Euroimmun  $\geq 6$ ).

We test all other potential donors with antibody tests prior to donation. The cut-off for accepting the potential donor for donation is a Euroimmun of 6 or above.

#### Question 7

Yes. We test all units prior to issue for anti-SARS-CoV-2 antibodies. The cut-off for use within the trials is a Euroimmun of 6 or above. All other units with positive antibody tests that do not meet this criterion are currently being stored. Additional samples on the CCP issued for use have been archived in case a better test for assessing the quality of a convalescent plasma sample is developed in the future.

#### Question 8

No. We do not use any pathogen reduction treatments on our convalescent plasma components or our plasma components.

#### Question 9

Yes. We started accepting recipients of CCP as convalescent plasma donors but not as donors for any other blood components. Our first donor who has received CCP has donated and had high anti-SARS-CoV-2 antibody levels (Euroimmun 20).

#### Question 10

Yes. We accept individuals who have recovered from COVID-19 infection as standard whole blood or platelet apheresis donors. They must have recovered from COVID-19 at least 28 days prior to donating.

#### Question 11

No. Individuals who have received CCP during their illness are unable to become standard whole blood or platelet apheresis donors.

#### Question 12

We have achieved a lot over the last few months. Rolling out a national convalescent plasma programme has required a huge amount of work by a large number of participants. We have opened 20 new donor centres over the last year to enable collection of convalescent plasma.

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## South Africa – Western Cape Blood Service

Vernon Louw

#### Question 1

Type of institution.

○ Regional Blood Services/Blood Centre (responsible for recruiting donors; screening and selecting blood donors; blood collection; testing and processing blood units; transporting; receiving and storage of blood units; pre-transfusion testing, and issuing blood for clinical transfusion at a regional level)

Institution demographics.

Whole blood donations 147 684, Platelets 9265, Plasma 38 000.

#### Question 2

Only plasmapheresis.

Every 2 weeks, i.e. 24 × per year.

#### Question 3

Only for trial use.

#### Question 4

SARS-CoV-2 PCR and/or antigen test and/or SARS-CoV-2 Ab positive.

14 days post last symptoms or asymptomatic since test

#### Question 5

No.

#### Question 6

Yes, but donation allowed before results available.

#### Question 7

Yes.

*Question 8*

Yes, Terumo technique (riboflavin)

*Question 9*

Yes, in theory, no such rules, but 3-month deferral.

*Question 10*

Yes.

*Question 11*

Yes, after 3-month deferral.

*Question 12*

Concerns about the risk of attending a blood collection centre.

Many staff members off-sick from COVID during this period, adding to the high workloads.

Putting in place protocols to ensure staff and donor safety.

Outbreaks of COVID-19 among staff or exposure of staff to COVID patients leading to quarantining and being off work.

Management of staff working remotely.

Decrease in blood drives and blood stocks.

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