NHS
Blood and Transplant

COVID-19 Convalescent Plasma

Training Slides

Caring Expert Quality

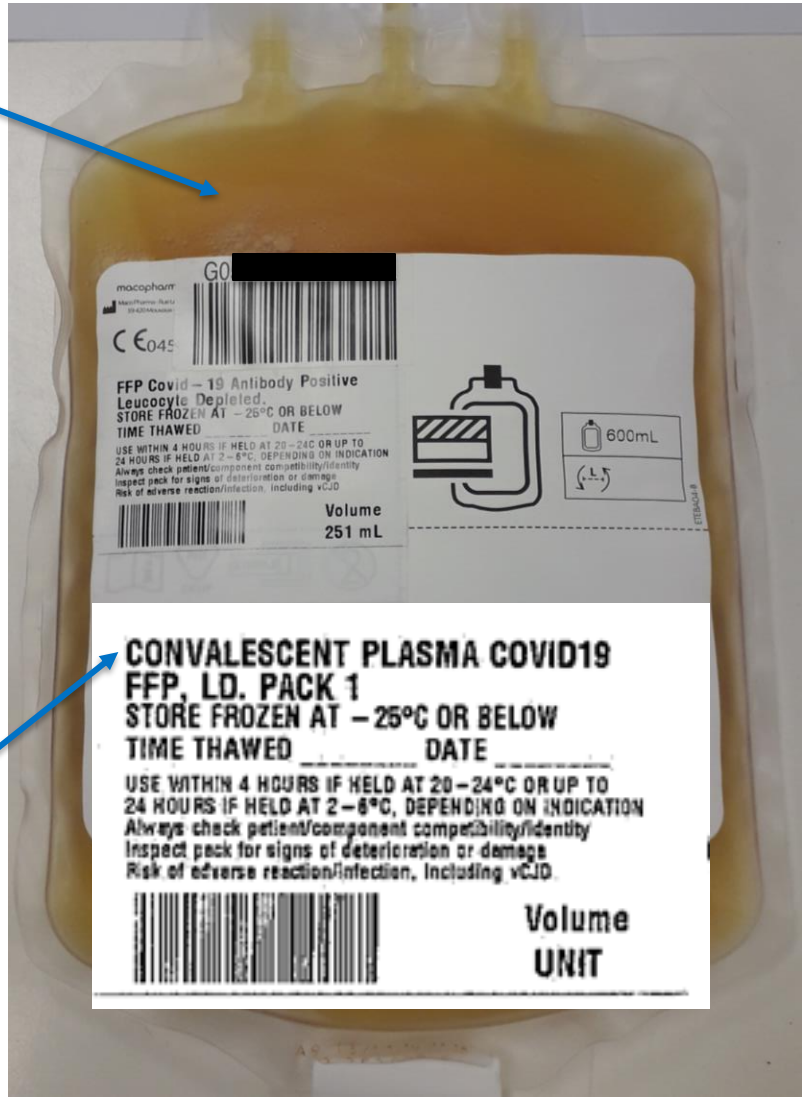
Convalescent Plasma COVID19

NHS Blood and Transplant

Unique identifier: G no

Convalescent plasma COVID-19 FFP is plasma donated from patients who have recovered from COVID-19 and contains antibodies to help fight COVID-19.

This is a new product and **must ONLY be used for the REMAP-CAP trial.**



Labelled Convalescent Plasma COVID19

REMAP-CAP

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- Randomized, Embedded, Multifactorial Adaptive Platform trial for Community-Acquired Pneumonia
- Multicentre trial recruiting across UK Hospitals (ICUs)
- Convalescent plasma will be administered as part of the REMAP-CAP Immunoglobulin (including Convalescent Plasma) therapy domain only
- Patients will be randomised to receive one of two open label interventions (1:1):
  - no immunoglobulin against COVID-19 (no placebo)
  - convalescent plasma

REMAP-CAP Immunoglobulin (Convalescent Plasma) Domain

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- Patients receive two adult units of ABO compatible convalescent plasma (total volume 550ml ± 150ml)
- 2 units administered to maximise potential for patients to receive high antibody levels
- within 48 hours of randomisation
- minimum of 12 hours between transfusions
- The second unit of Convalescent Plasma should be from a different donor.

Eligibility

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Patients will be randomised to REMAP-CAP on admission to ICU if they meet the eligibility inclusion criterion:

- COVID-19 infection confirmed by microbiological testing

And none of the domain specific exclusion criteria:

- It has been > 48 hours since ITU admission
- It has been >14 days since hospital admission
- Patient has received antibody therapy against COVID-19 (convalescent plasma, hyperimmune globulin, monoclonal antibody)
- Patient has previous history of TRALI
- Patient has known moderate/severe allergy to blood components
- Patient has known objection to receiving plasma containing components
- Contraindication / clinician decision

Randomisation

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- Randomisation performed on REMAP-CAP platform by research team
- Includes COVID-19 Immunoglobulin domain randomisation
- Patient allocated with unique trial ID (10 digits)
- If a patient is randomised to the intervention arm - notify transfusion laboratory that the patient has been randomised to receive convalescent plasma ASAP.
- Provide transfusion laboratory with unique patient trial ID number

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REMAP-CAP Training Material available here:

https://www.icnarc.org/Our-Research/Studies/Remap-Cap/Information-For-Sites/Training

Hospital Stock

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- **DO NOT ORDER THE FIRST UNITS OF CONVALESCENT PLASMA. NHSBT will liaise with you and order the convalescent plasma for you.**

- Prior to the green light to start recruiting to the REMAP-CAP Convalescent Plasma domain each site will be given a stock of:
  - ~2 Units of A
  - ~2 Units of O
- Units of AB and B will be ordered on a case by case basis

- Convalescent Plasma has its own unique product code *(barcodes on next slide)*

- This stock must be stored in the transfusion laboratory **separately from other blood products** at -25°C

- Subsequent stocks can be ordered from the OBOS system: OBOS@nhsbt.nhs.uk

- **Convalescent plasma must be issued for TRIAL USE ONLY**

- Please consider logistics and weekend cover

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Component description	NHSBT Pulse Code	Start Code	Barcode No.	Stop Code	Barcode
CONVALESCENT PLASMA COVID19, FFP, LD Pack 1	CHP1	a0	37861	3b	a0378613b
CONVALESCENT PLASMA COVID19, FFP, LD Pack 2	CHP2	a0	37862	3b	a0378623b
CONVALESCENT PLASMA COVID19, FFP, LD Pack 3	CHP3	a0	50050	3b	a0500503b
CONVALESCENT PLASMA COVID19, FFP, LD	CHP4	a0	37863	3b	a0378633b

Scotland

NHS Blood and Transplant

- Sites will order 2 units of convalescent plasma when required
- This will be ordered from the local manufacturing site by phone/fax
- CP has its own unique product code
- This stock must be stored in the transfusion laboratory **separately from other blood products** at -25^{o}C
- **Convalescent plasma must be issued for <u>TRIAL USE ONLY</u>**
- Please consider logistics and weekend cover

Wales

Gwasanaeth Gwaed Cymru
Welsh Blood Service

- Each site in Wales will be required to register for the REMAP-CAP study in order to receive CP
- WBS will hold a stock of CP (all ABO groups) that meet the specification criteria of the REMAP-CAP study
- Hospital Transfusion labs (HTL) involved in the trial will either:
  - be provided a small stock to issue as required (larger health boards) or
  - order direct from WBS when needed (smaller health boards).
- CP will be issued to the HTL using a new order form* (to be issued imminently).
- Named basis for requesting is not required, but ABO group will be requested
- The stock must be stored in the transfusion laboratory **separately from other blood products** at – 25^{o}C
- Please consider logistics and weekend cover when ordering

*ETHOS may not be update in line with ‘Go Live’ therefore use of order forms maybe required initially

Convalescent plasma must be issued for **TRIAL USE ONLY**

NHS
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Northern Ireland

- Sites will order 2 units of convalescent plasma when required
- This will be ordered from NIBTS by fax
- Phone communication prior to ordering is welcomed
- CP has its own unique product code
- This stock must be stored in the transfusion laboratory **separately from other blood products** at -25^{o}C
- **Convalescent plasma must be issued for <u>TRIAL USE ONLY</u>**
- Please consider logistics and weekend cover

Issuing Convalescent Plasma

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- 1 unit of ABO compatible Convalescent Plasma thawed as per normal transfusion laboratory procedures (ABO matched if possible)(use standard grouping practice).
- Issue Convalescent Plasma via LIMS or other standard systems
- Each unit must be requested and issued as separate events.
- Laboratory staff must record the patient's trial number in the Convalescent Plasma Log/download via LIMS system. Provide to CTU@nhsbt.nhs.uk weekly.

Trial and Patient Trial ID	Donation ID of Issued Convalescent Plasma	Date and Time Issued	Issuer Name	Confirmed Fate of Unit T Transfused W Wasted S Split/Damaged R Re-issued
REMAP-CAP ☐ RECOVERY ☐ Relevant Trial ID:	G_ _ _ _ _ _ _ _ _ _ _ _ _ _ Pack No: ___	__/__/____ :		
REMAP-CAP ☐ RECOVERY ☐ Relevant Trial ID:	G_ _ _ _ _ _ _ _ _ _ _ _ _ _ Pack No: ___	__/__/____ :		

Transfer of Convalescent Plasma

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- Yellow trial bags provided for transfer of the unit to the ward.
- Convalescent Plasma transferred to ICU following local procedures and transfused within 4 hours of thawing if stored at room temperature or within 24 hours of thawing if stored at 4 C.
- Convalescent Plasma to be transfused as soon as possible

Administration

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- All administration bedside transfusion safety checks must be undertaken.

- Donation number (G no), volume transfused, and start and finish date and time of transfusion should be documented on the eCRF and patients medical notes by the research team. Infusion rate as per standard practice.

- Patients can receive other blood components, as required.

- There must be a minimum of 12 hours between transfusions* and both units should be given within 48 hours of randomisation.

*Provided the patient has not had any serious adverse reactions, the research team will request a second unit from the transfusion laboratory.

- Ensure timely communications to laboratory staff to facilitate this.

Transfusion Related Adverse Reactions

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- All transfusion-related serious adverse events / reactions are reportable to SHOT/SABRE.
- Other reportable events include: wrong component transfused (includes patients given standard FFP instead of convalescent plasma)
- ICU staff to inform blood bank/transfusion practitioner of any serious reaction immediately.
- Reports to SHOT/SABRE ASAP (preferably within 48 hours) by transfusion teams.
- Must include trial name and patients trial number on the SHOT reporting system in addition to the other details of the reaction.
- Tx related SAE/SARs should also be reported on form 11 of REMAP-CAP eCRF.
- If at any point during the transfusion the patient has a serious reaction, the transfusion should be stopped as per clinician's decision and appropriate investigations and treatment initiated.

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SHOT
Serious Hazards of Transfusion

For other useful resources, please visit www.shotuk.org/resources/current-resources

Domain Specific Outcomes

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- All-cause mortality at 28 days
- SAEs
- Percent of subjects who cleared SARS-CoV-2 infection – through RNA testing
- Reduction in SARS-CoV-2 viral load – from blood and respiratory samples
- Change in SARS-CoV-2 neutralising antibody levels - from blood samples
- Number of thrombotic events from randomisation up to the end of study day 90

For sites taking part in sampling sub-study:

NHS Blood and Transplant

- Follow Laboratory SOP (INTENSIVE SAMPLING). All samples require storage in -80°C freezer (or if unavailable, -20°C). Link to SOP.
- Supplies will be provided by the Research Laboratory Team [remap-plasma@kcl.ac.uk].

	Week 1							Week 2							Week 3							Week 4						
Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
Blood (EDTA) 2ml	*			*																								
Blood (EDTA) 4ml	*	*	*	*		*			*			*			*													*
Blood (serum) 6ml	*	*	*	*		*			*			*			*													*
PAXgene 2.5ml	*								*																			
Nasopharyngeal ***or*** Oropharyngeal swab	*	*	*	*		*			*			*			*													*

Overview:

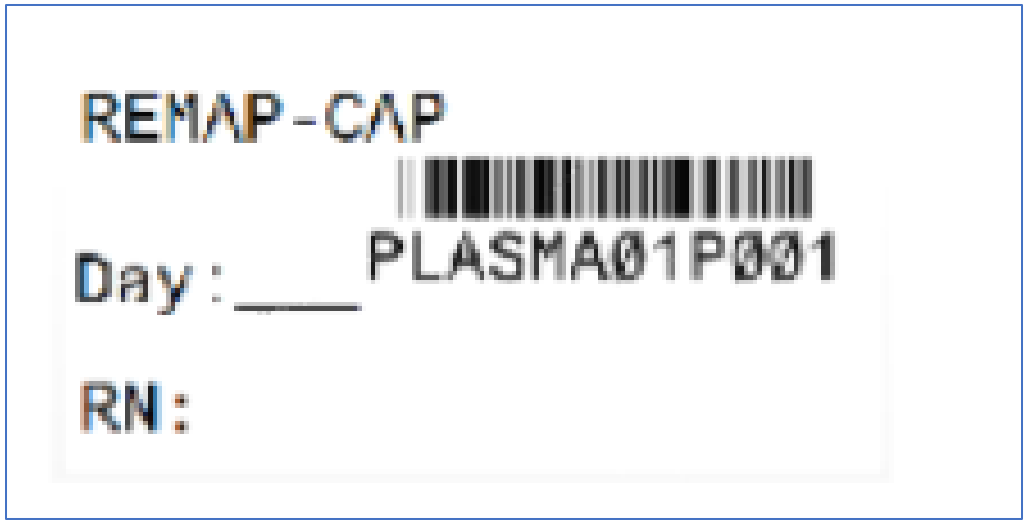
NHS Blood and Transplant

Sample		Timepoints	Initial processing	Aliquots
	Blood sample (EDTA) – 2ml	**2** (D1, D3)	BEFORE COLLECTION: aliquot 500µL of blood stabiliser into 4 cryovials (10 mins prior to collection). Within 2 hours of collection, transfer 500µL of blood to each cryovial. Mix well.	After 10 minutes, freeze at -80 °C*.
	Blood sample (EDTA) – 4ml	**9** (D1, D2, D3, D4, D6, D9, D12, D15, D28)	Centrifuge 1100g-1300g for 10mins (within 2 hrs of collection (max. 4 hours)).	Supernatant: Aliquot 250-500µL and freeze at -80°C*
	Blood sample (serum) – 6ml	**9** (D1, D2, D3, D4, D6, D9, D12, D15, D28)	Store upright at room temperature for 30-60 minutes, then centrifuge 1100g-1300g for 10 mins (centrifuge temp: room temp).	Supernatant: Aliquot 250-500µL and freeze at -80°C*
	Blood sample (PAXgene) – 2.5ml	**2** (D1, D9)	Store upright at room temperature for 2-6 hours, then freeze at -80°C*	Freeze at -80 °C*
	Nasopharyngeal / Oropharyngeal swab	**9** (D1, D2, D3, D4, D6, D9, D12, D15, D28)	Do not process	Double-bag and freeze at -80 °C*

*if -80°C freezer not available, samples can be stored at -20°C instead.

All samples will be transferred to the core laboratory (based at Guy's Hospital) on a weekly basis throughout the trial.

Labelling



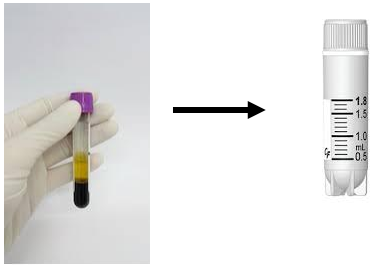
- Pre-printed labels will be provided.
- REMAP-CAP randomisation number must be added to each label.

Plasma

- Collect one EDTA Blood Collection Tubes for plasma (4mls of blood)
- Mix the blood gently by inverting the collection tubes 8 to 10 times
- Send to pre-agreed sample processing area

- Centrifuge ideally within 2 hours* of collection **(IMPORTANT)**
  - 10 minutes
  - 1100-1300g (*NOTE: DO NOT EXCEED centrifuge speed over 1500 g)*
  - Room temperature

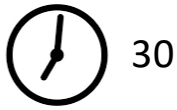
- Use a pipette to transfer the plasma into the labelled cryovials
  - Each aliquot volume ranges between 250 microlitres and 500 microlitres.
  - Close the caps on the vials tightly.
  - This process must be completed within 1 hour of centrifugation.
- All specimens should remain at -80^{o}C prior to shipping.



Serum

- Collect **one** Blood Collection Tubes for serum (~6 mls of blood)
- Send to pre-agreed sample processing area

- **Allow clot to form** by keeping the filled blood collection tubes (vacutainers) upright, after the blood is drawn,
- at room temperature (18°C-25°C)
  - for 30 - 60 minutes to allow the clot to form **(IMPORTANT)**

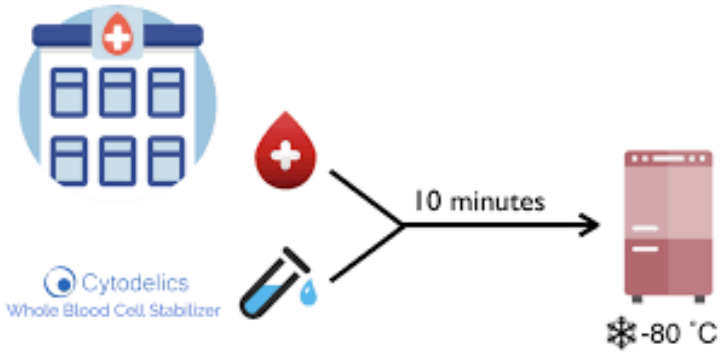


- **Centrifuge** the blood samples at the end of the clotting time as follows
  - 10 minutes
  - 1100-1300g (*NOTE: DO NOT EXCEED centrifuge speed over 1500 g)*
  - Room temperature

- Use a pipette to transfer the serum into the labelled cryovials
  - Each aliquot volume ranges between 250 microlitres and 500 microlitres.
  - Close the caps on the vials tightly.
  - This process must be completed within 1 hour of centrifugation.
- All specimens should remain at -80°C prior to shipping.

Cell Aliquots

- Collect **one** EDTA Blood Collection Tube (2mls of blood)
- Mix the blood gently by inverting the collection tubes 8 to 10 times
- Send to pre-agreed sample processing area



- **BEFORE** blood collection (includes labelling)
  - Label 4 cryovials with stickers provided
  - Aliquot 500ul of cytodelics blood stabiliser to each
  - Allow 10 minutes to equilibrate to room temperature
  - (This can be done in advance)

- **AFTER** blood collection (within 2 hours)
  - **IMPORTANT -** invert 2ml EDTA tube 6-8 times.
  - Transfer 500ul into each cryovial.
  - Mix well by inverting 15 times (DO NOT vortex)
  - Incubate at room temperature for 10 minutes

- Place in Eppendorf box and store in -80 freezer.
- All specimens should remain at -80^{o}C prior to shipping.

PAXgene RNA

- Label PAXgene Tube with stickers provided
- Collect one PAXgene Blood RNA Tubes at two pre-defined time points.
  - Hold the PAXgene Blood RNA Tube vertically. Allow at least 10 seconds for a complete blood draw to take place. Ensure that the blood has stopped flowing into the tube before removing the PAXgene Blood RNA Tube from the holder.
  - Gently invert the PAXgene Blood RNA Tubes 8 to 10 times. **(IMPORTANT)**
  - Store the PAXgene Blood RNA Tubes upright at room temperature (18°C-25°C) for a minimum of 2 hours. The tubes can be left at room temperature for a maximum of 24 hours
- Transfer the tubes to a -80°C freezer for storage until shipping.
- All specimens should remain at -80°C prior to shipping.

Virology Samples

- Collect either an oropharyngeal **OR** nasopharygeal swab.
- Double bag the sample after collection **(IMPORTANT)**.
- Store in minus 80^0C in the double bag until transport

For sites not taking part in sampling sub-study:

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- Baseline (Day 1) samples only:
  - 1 x 6mL serum blood sample (yellow/red or equivalent tube for serum)
  - 1 x Nasopharyngeal or Oropharyngeal sample

- Labelling samples:
  - REMAP-CAP Randomisation Number
  - Date/time of sample collection
  - Sample type

- Refer to Laboratory SOP (BASELINE ONLY SITES) – link here

- Postage kits provided by NHSBT CTU (CTU@nhsbt.nhs.uk)

Sample Tracking and Transport

NHS Blood and Transplant

- Complete Sample Tracking Form (**away from clinical area**), this must be sent with the samples in the SafeBox

REMAP-CAP

Sample Tracking Form

Please complete this form and send with samples.

Hospital Site: _____			REMAP-CAP Randomisation Number: _____
Sample type	**Sample collected? (enter a cross in the box)**	**Date Posted**	**Comments**
Serum tube x 1	☐YES ☐No		
Nasopharyngeal swab	☐YES ☐No		
Oropharyngeal swab	☐YES ☐No		

Each sample should be labelled with: REMAP-CAP randomisation number, date sample collected, time sample collected, type of sample.

Name	
Signature	
Date	

LABORATORY USE ONLY	
Date received/processed:	

- Samples should be posted to King's Core Lab (using SafeBoxes supplied)
- Both samples (blood & respiratory) in same box, plus Sample Tracking Form
- Email REMAP-plasma@kcl.ac.uk after posting and add to the log (Local Sample Tracking Log)

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Important Note

No samples should be transferred to the Research Laboratory until an appropriate form of written consent is in place (e.g. professional legal representative)

Training Attendance

NHS Blood and Transplant

- Please email **CTU@nhsbt.nhs.uk** to confirm you have attended the training.
- Training can be cascaded – please email once you have read the slides.
- Key documents available here:

www.nhsbt.nhs.uk/covid-19-research/documents-and-downloads

Thank you!