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WMDA matching donors • serving patients

# Welcome to the EBMT/WMDA webinar

*How to ensure unrelated donor grafts and CAR-T Cell Products during the Corona pandemic*

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# Welcome on behalf of EBMT

Nina Worel, chair EBMT Donor Outcome Committee

# Introduction

- Bronwen Shaw, CIBMTR
  *Welcome on behalf of WMDA*

- Mirjam Fechter, Medical Director Matchis Foundation/Medical Consultant WMDA
  *How to ensure donor safety in time of COVID-19?*

- Ann O'Leary, Assistant Director Donor and Transplantation Services Anthony Nolan
  *UK-perspective on donor motivation and donor availability*

- Gabi Rall, Director Medical Business Development DKMS
  *Transport, Health and Availability Check (HAC) and workup in time of COVID-19*

- Christian Chabannon, Chair Cellular Therapy and Immunobiology Working Party of EBMT
  *How to ensure CAR-T Cell therapy in time of COVID-19?*

# Learning Objectives

- To inform healthcare professionals about the current state of knowledge regarding the COVID-19 pandemic and its impact on the provision of unrelated stem cell transplants as of 6 April, 2020
- To identify good sources of information in the area of donor care in the COVID-19 pandemic
- To relay our current understanding of the impact of COVID-19 on transport, and provision of CT samples and stem cell products
- To know what you can do as healthcare professional to get an unrelated transplant in your centre or to work on alternative solutions (e.g. cord blood transplant or cryopreserved products)
- To provide information about what EBMT and WMDA are doing in the COVID-19 pandemic

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# Welcome on behalf of WMDA

Bronwen Shaw, president-elect WMDA

# Continuity of Care – WMDA services for the BMT community

- Donor suitability criteria: https://share.wmda.info/x/ED6OF

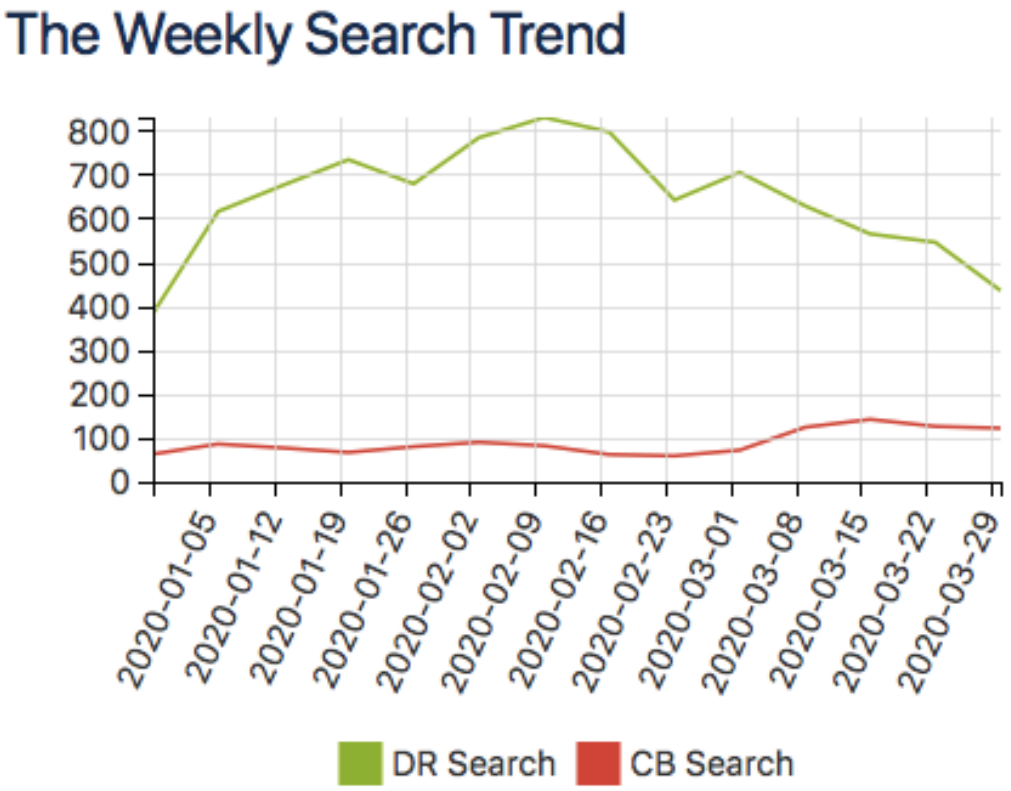
- Transport waivers for exchange of products between countries
  - European waiver for exchange of products to and within Europe
  - US waiver for exchange of products to and from United States

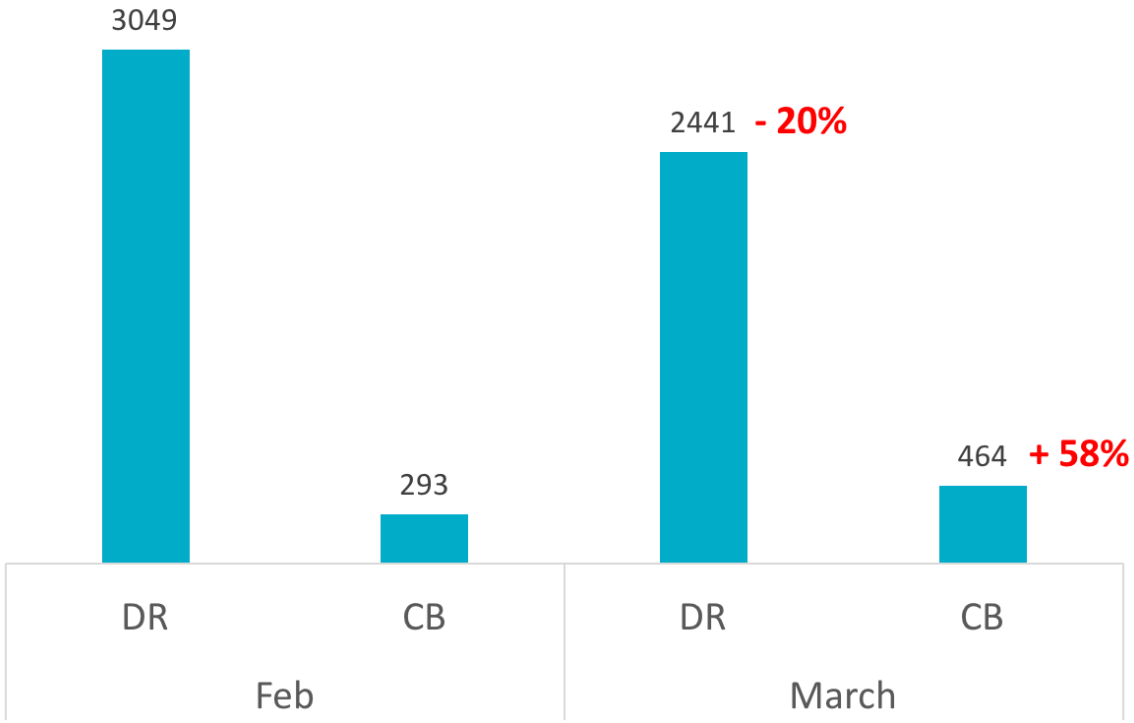
- Webinars on how countries work on solutions
  - Germany, ZKRD: https://youtu.be/LKJHMDx8pcI
  - Italy, Italian BMDR: https://youtu.be/6AYeJJXnvtg

- Webinars to provide information
  - Medical: https://youtu.be/JGq7B_sUPHQ
  - Emergency Task Force: https://youtu.be/ccutfk0o448
  - Cord Blood Selection Service: https://youtu.be/LKJHMDx8pcI

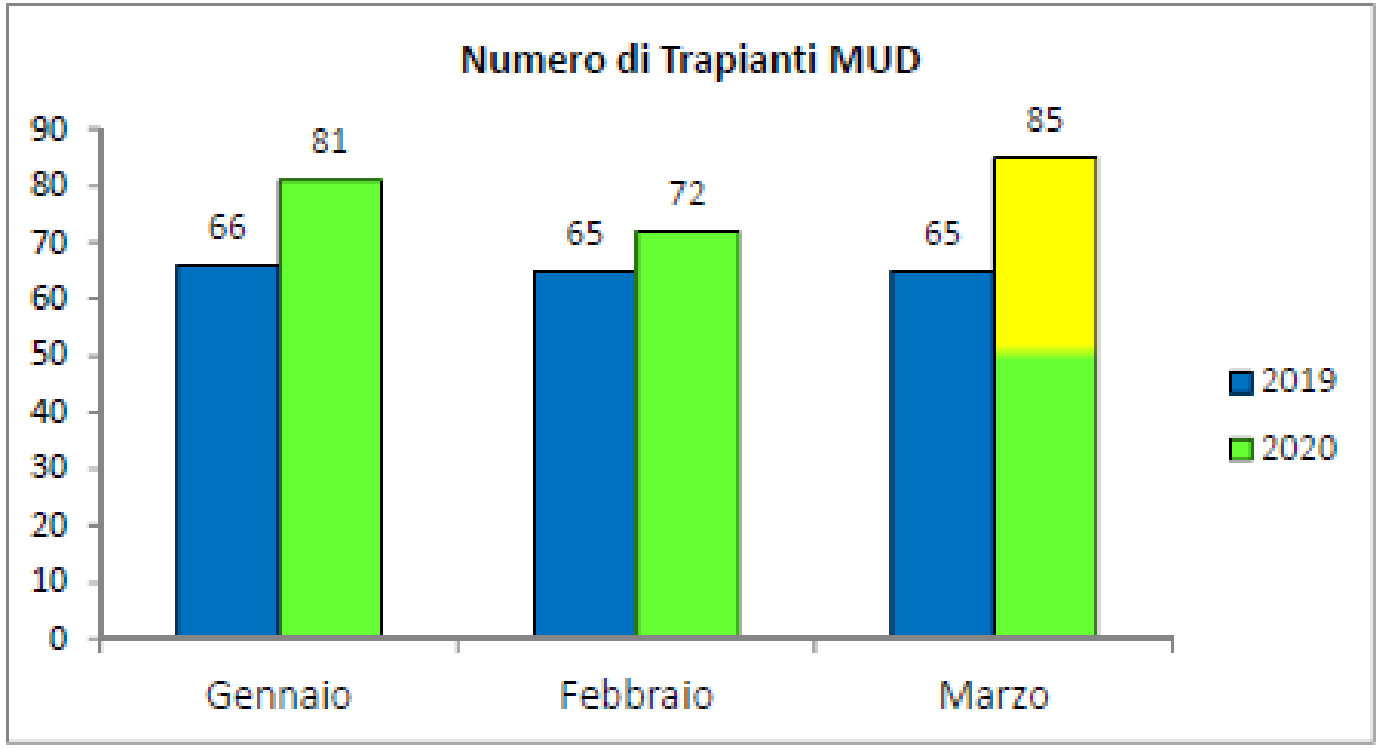
- Country specific information how registries ensure provision of stem cells and what their potential limitations are, visit: https://share.wmda.info/x/Yj6OF

# Number of searches in WMDA Search & Match per week



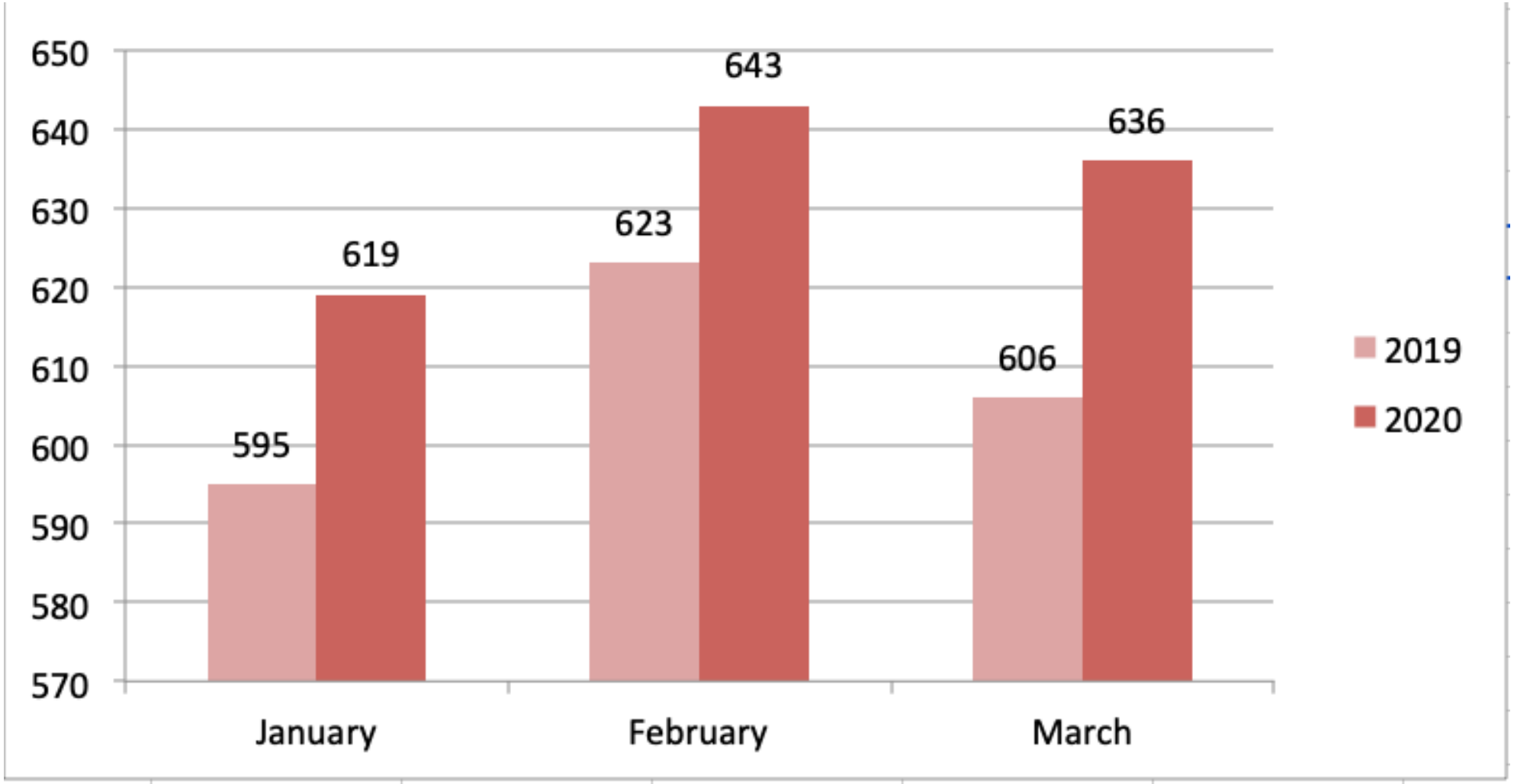



# Experience from the Italian BMDR

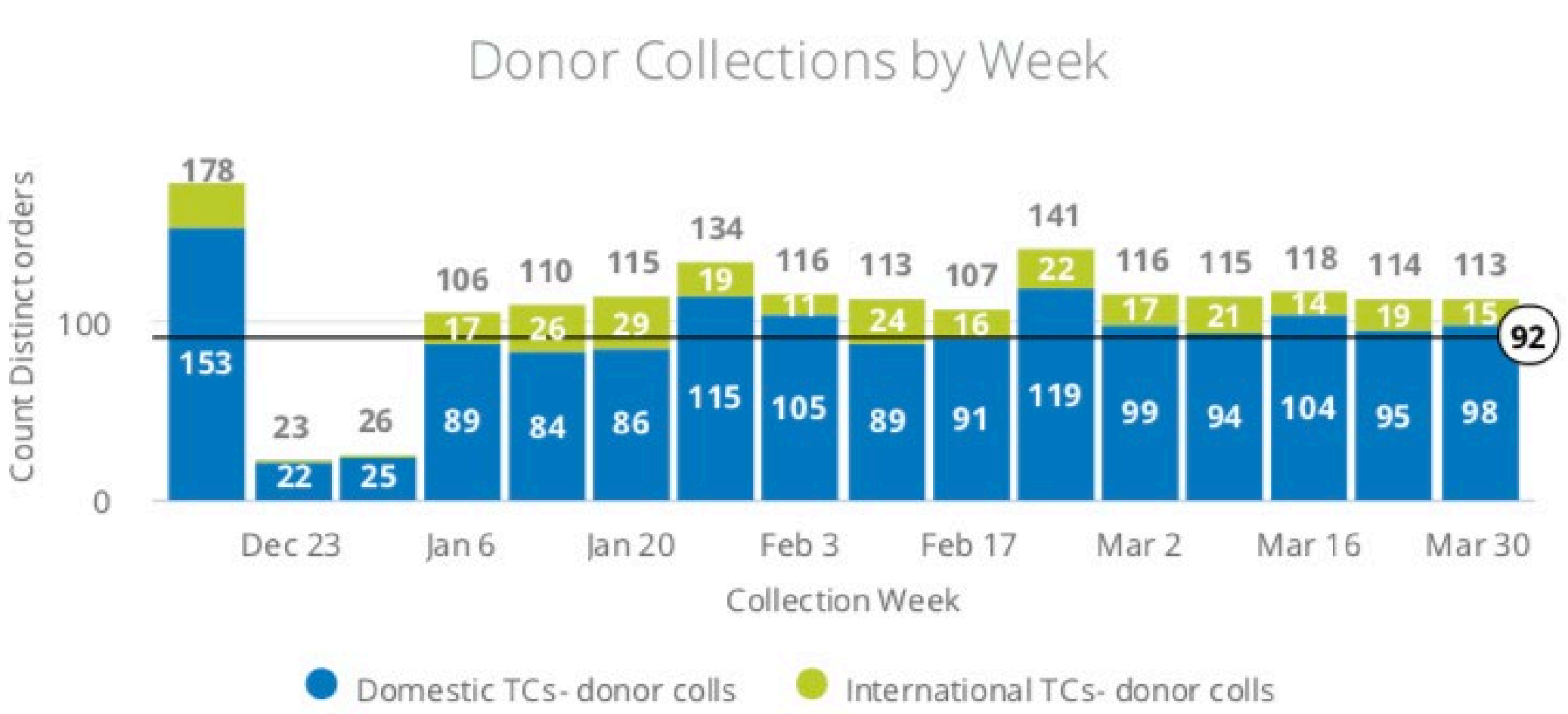



*Presentation by Nicoletta Sacchi, Italian BMDR (April 2, 2020); watch: https://youtu.be/6AYeJJXnvtg*

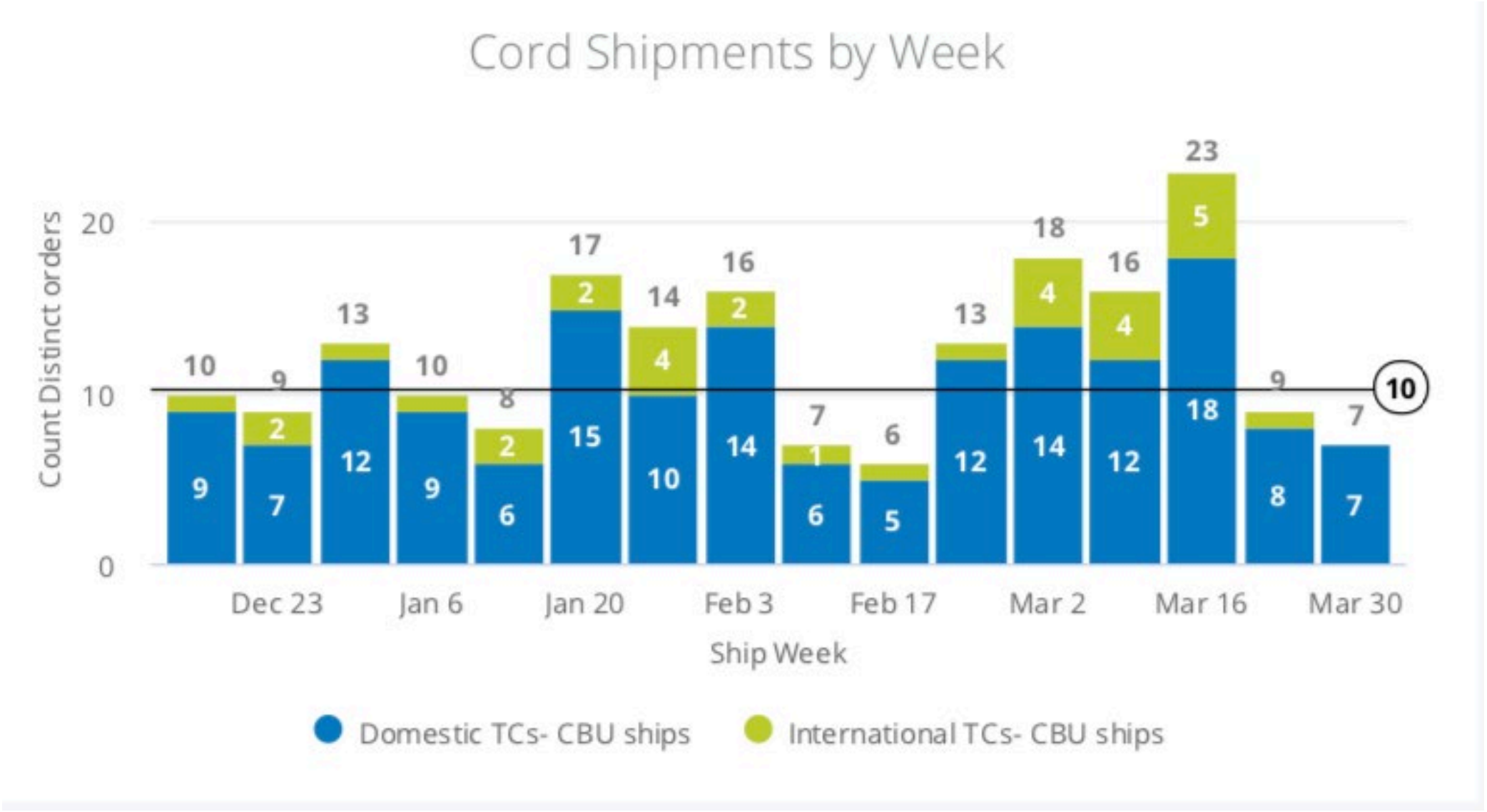
# Experience from the DKMS



# Experience from the NMDP



# Number of CB shipped by NMDP



# WMDA Quick Survey – WMDA registries

| No. of cancellations due to COVID-19 pandemic | Donor | Collection centre capacity | Transplant centre |
|---|---|---|---|
| Belgium | 1 worried<br>1 not eligible | | |
| Greece | 2 travel<br>4 worried | 1 | 2 |
| Lithuania | 1 worried | | |
| Portugal | | 5 | |
| Switzerland | | | 2 |

No COVID-19 cancellations reported from:
Croatia, Czechia, Denmark, Finland, Netherlands, Norway, Serbia and Sweden

Most registries report a drop down between 0-30%
Canadian registries report a drop down of 50%
Portugal and Greece report a drop down of >70%
14 requests were postponed

# The Cancer Letter from DKMS and NMDP

In order to further ensure patient safety, most international registries are now strongly recommending that unrelated donor products be collected prior to initiation of patient conditioning. This will guarantee the donor graft is available on the intended day of transplantation.

In fact, the NMDP has just made cryopreservation prior to conditioning a requirement, and others may follow suit.

Collectively, the volunteer unrelated donor community, together with the transplant centers, is working collaboratively day and night to continue uninterrupted our commitment to connect these remarkable donors with their patients.

We are still receiving many requests for unrelated donor products, as transplant centers continue to believe this is in the best interests of their patients.

**Against all odds**

**Unrelated stem cell transplants in coronavirus times**



https://cancerletter.com/articles/20200327_7/

# Upcoming webinars

**Tuesday, April 7th (13:00 CEST): NMDP - ensuring continuity of care and sharing experiences**,
*by Steven Devine - NMDP*

**Thursday, April 9th (12:00 CEST): Singapore BMDP - ensuring continuity of care and sharing thier experience**,
*by Charles Loh, Elaine Tan and Louise Cho*

**Tuesday, April 14th (14:30 CEST): Gift of Life Marrow Registry - ensuring continuity of care and sharing their experience**,
*by Jay Feinberg, Marti Freund and Amy Glanzman*

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# SARS-CoV-2 and COVID-19

## *The WMDA position on donor care and assessment*

Mirjam Fechter, Medical Consultant WMDA

*Hung Yang, Chair Donor Suitability Committee*

# Donor suitability

- Focus on donor safety; *consider possible transmittability via blood/stem cells*

- Risk factors:
  - Contact with COVID-19 patient
  - Recent international travel (esp via air & sea)

- Deferral period when risk factors are present
  - If feasible: 14-28 days (twice the median or maximum incubation period)

- Testing for SARS-CoV-2:
  - For any fever or respiratory symptoms – yes
  - Otherwise - WMDA does NOT recommend

# Routine screening for SARS-CoV-2

- No licensed test for blood or HSC yet.
- CoV (has receptors) in nasopharynx ≠ CoV in blood/stem cells.
- Swabbing all donors for SARS-CoV-2 **prior to donation** (e.g. at work-up or before G-CSF) has some potential value:
  - It may prevent an incubating donor from getting G-CSF & exposing staff to pre-symptomatic COVID-19.
  - It may provide early warning that the donation will not proceed.
- However, routine testing is hard to justify if community risk is low and/or testing capacity is limited.
- Swabbing all donors for SARS-CoV-2 **on the day of donation** has no value, because:
  - It does not prevent harm to the donor, who has donated by the time a result is known.
  - It does not prevent harm to the recipient, because there is no evidence for pre-symptomatic viraemia.

# Donor care

- Minimize exposure risk:
  - Urge donors to follow government guidelines/rules and persuade them to do even better
  - Avoid public transport
  - Follow strict hygiene measures and social distancing and make sure phlebotomy and collection facilities do the same
- Regular screening for symptoms
  - Prior to start conditioning, prior to and during mobilization, collection
- At minimum:
  - Test when symptomatic, interrupt or stop mobilization when concern for donor safety
- Post donation screening for symptoms only
- Report adverse events!
- Quarantine of product is NOT recommended by WMDA

# Post-donation quarantine (1)

- **Routine cryopreservation**, which is now generally allowed and even recommended**,** allows patient conditioning to be deferred until successful collection can be confirmed in COVID-19 crisis conditions.

- This inherent delay appears to allow for, but is not the same as a "**quarantine period**" whereby product is not used unless a defined incubation period (e.g. 14 days) elapses and:

  - *The donor remains symptom-free, or*
  - *The donor tests negative for SARS-CoV-2*

# Post-donation quarantine (2)

- WMDA does not recommend this practice because:
  - The donation could have **preceded** the infection
  - If a donor **develops symptoms of COVID-19 after donating**, then the donation was collected during the pre-symptomatic period (or before). While there is evidence of respiratory infectivity during the pre-symptomatic period, that does not equate to viraemia
  - If a symptomless donor **tests positive to SARS-CoV-2 on Day 14+**, the possibility of pre-symptomatic infection on Day 0 is effectively excluded
  - Therefore discarding a donation for failed quarantine is **detrimental to the patient** because they lose their first-choice donor
  - It is also **detrimental to the donor** because their exposure to G-CSF, apheresis and unnecessary COVID-19 community risk is wasted.
- Of course (local) law and regulations will always take precedence.

# Evidence base

- Receptors in airways; pulmonary tropism
- Very low level of viraemia in some symptomatic patients (1-15%)
- No detected viraemia in incubation period or asymptomatic patients
- So far, **no evidence** of transmission through blood or HSC products of SARS-CoV-2 nor for other corona or non-latent respiratory viruses.

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# UK-perspective on donor motivation and donor availability

Ann O'Leary, Assistant Director Donor and Transplantation Services Anthony Nolan

# UK experience – donor support and availability

Donor health and safety is our priority and we've put a number of steps in place to support donors:

- FAQs for staff to provide donors with the answers they need
- Donor information to provide them with facts and to reassure (as far as possible)
- Revised donor health history questionnaire and testing policy
- Deferring donors who are classed by UK government as part of an 'at risk' category (e.g. asthma)
- Working with our collection centres to ensure every precaution is taken to ensure that risk to donors is minimised
- Adapted travel and accommodation itineraries
- Removed the requirement for blood samples at VT

Saw an increase in need for support for donors over February / March 2020

# We are seeing some reluctance at the VT stage…

‘Donor doesn’t feel comfortable going to a medical facility during the pandemic’

‘Both donor’s parents are in self-isolation due to being in high risk groups, so donor does not want to proceed’

‘Donor’s wife is 7 months pregnant and he has asked to be made temporarily unavailable’

‘With the current situation, donor wasn't comfortable with going ahead’

‘Donor’s husband is a key worker and she has two young children who are currently dependant on her’

‘Donor is an intensive care nurse and has decided she shouldn’t proceed at present’

However, donor availability for Feb / March was still more than 60%

# Many challenges at workup, including:

Increased deferrals due to ‘at risk’ conditions

Donors testing positive for COVID-19

Small number of donors who feel at the moment that they cannot go ahead with the donation

Donors who are based in remote areas of the UK, where travel is currently impossible

# Despite these challenges:

February and March 2020 were Anthony Nolan's busiest two months for provision ever

Imported cells from 13 countries and exported cells to 16 countries

Identified back up donors / cords for UK patients (H&A check)

Each donor is treated and supported as an individual, addressing their specific needs and concerns

We are still facilitating collections every day

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# Transport, Health and Availability Check (HAC) and workup in times of COVID-19

Gabi Rall, director medical business development DKMS

# How to ensure transport in times of COVID-19?

Europe:

Even though borders are closed, transports within Europe are possible in most cases as there are exemptions on many borders

- Handover of products at the border Poland/Germany; Slubice/Frankfurt Oder
- Hub at the Heathrow Airport in London
- Hubs in Airports in Spain and Italy

EU legislation on transport of cells and cross borders

# How to ensure transport in times of COVID-19?

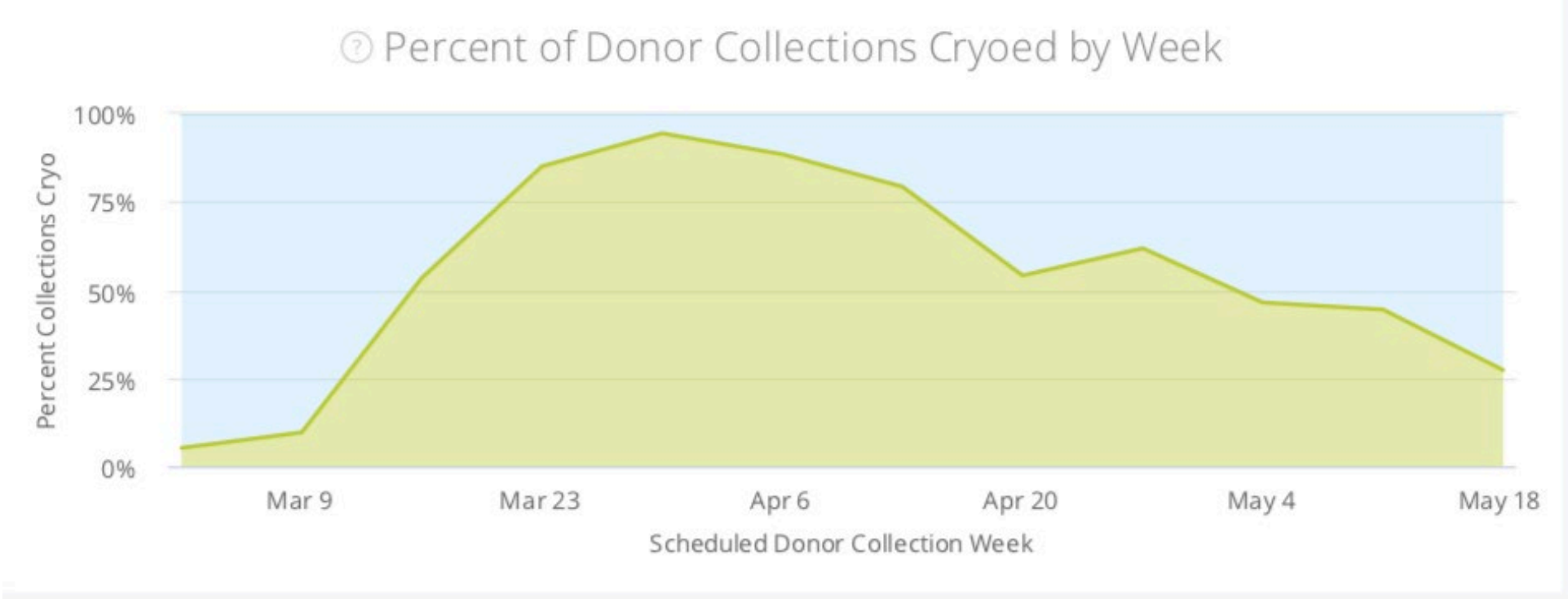
- Together, time:matters, NMDP, ZKRD, DKMS and WMDA have developed a possible Cargo solution where fresh products can be shipped in the cockpit of the aircraft from Frankfurt to the US
- Two test shipments of blood samples have been successfully performed
- NMDP and DKMS have agreed that, starting April 6$^{th}$, all products from DKMS will be shipped using this solution, as Cargo flights are the most stable flights and the number of Cargo flights has increased

# How to ensure transport in times of COVID-19?

Cryopreserved Shipments

- Cryopreservation is recommended these days
- This could be the last option if no passenger flights are available or couriers do not get a waiver to enter a country
- Many registries do have experience with cord blood shipment
- Cord blood banks to support in case a registry does not have the experience to ship or receive a product
- TC’s need to accept cryo products

# Cryopreservation of products in the USA




*Source: NMDP*

# What is the Health and Availability Check (HAC)?

More and more DC/Registries are facing problems with blood draws:

People are forced to not leave the house

Donors are afraid to go to a blood drawing site

Doctors/Laboratories refuse to draw blood

→ **Implementation of a Health and Availability Check (HAC)**

# Health & Availability Check (HAC)

Detailed information session with the donor on the phone

HHQ with screening for Covid-19

Check availability and product preference

Report back results to TCs and Registries

TC can start workup whenever needed and CT/VT samples are drawn at medical examination

# Workup

BM collection capacities might collapse due to staff reasons, need for ICU beds, or availability of ventilators at short notice.

Therefore, in the current situation BM products should be reserved for those patients where PBSC is no option, especially small children and recipients with non-malignant conditions.

We strongly recommend to switch any bone marrow request to PBSC where medically feasible.

We will still accept BM requests, and do everything possible to continue, but we can no longer ensure that we will be able to collect this product to the same extent as we could for PBSC.

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# How to ensure CAR-T Cell Therapy in time of COVID-19?

Christian Chabannon, Chair Cellular Therapy and Immunobiology Working Party of EBMT

# CAR-T CELLS during the COVID-19 pandemic

Two aspects to be considered:

- Patient management
- Supply chain

# Patient management (1)

- Indications
    - Indications are relapsed / refractory aggressive hematological malignancies
    - A key issue with autologous CAR-T cells is disease control during the turnaround time for medicinal product manufacturing (is bridging chemotherapy indicated and feasible?)
    - Deferral is an especially difficult question in this context

- Issues specific to clinical trials
    - Many products in development
    - Most trials if not all are on hold for new inclusions

# Patient management (2)

- Feasibility
    - Patient free of SARS-COV-2 infection
    - Patient needs to access the collection (apheresis) facility
    - Patient needs to access the Hematology ward
    - Patient needs to access ICU in case of high-grade side effects (CRS, ICANS & others)
    - Patient needs to access other hospital facilities (MRI or other)

# Supply Chain (1)

- So far appear to be minimally disrupted
    - Closely monitor information released by manufacturers, as the situation may rapidly evolve
    - Tight communication between hospitals and manufacturers is key at all steps of the manufacturing process, and can take advantage of the IT systems deployed by manufacturers
    - Key rule is as usual: wait for reception of the released medicinal product at the hospital pharmacy before starting lympho-depleting regimen

# Supply Chain (2)

- Check availability of all needed resourced:
    - Collection facility ability to collect autologous blood mononuclear cells
        - beware of potential shortages of equipment / disposables in the future
        - in-house or 3rd party
    - Shipment to the Central Manufacturing Organization
        - subcontracted by manufacturer
    - Manufacturing capacities
        - many facilities are based in the USA
        - new facilities soon opening in Europe
    - Shipment back to hospital
        - subcontracted by manufacturer

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# Questions?

# Question 1

Q: TCs increasingly request more than one donor at a time for work-up due to all current uncertainties. This further increases the workload of registries, DCs and CCs and it can be frustrating for donors. What is the recommendation of WMDA and EBMT?

*A: Workup requests for more than one donor during this COVID-19 crisis are permitted, but the Donor Center always needs to be informed that more than one donor has been requested and they need to know which is the preferred donor and which is the back up donor.*

# Question 2

Q: Do cryopreserved stem cells need x-ray exemption if they are being transported in a LN2 dry shipper?

*A: For cryopreserved shipment, cells must not be x-rayed. An accompanying letter should be added and experienced courier companies who are shipping cord blood should be used.*

# Question 3

Q: Do we have any data about the risk of G-CSF for donors who become Covid positive during G-CSF?

*A: From previous reports and published data we know that G-CSF can induce an increased immune response causing an exacerbation of (auto-)immune related illness. So far, the WMDA has not received reports about donors who became SARS-Cov-2 positive during G-CSF and experienced more severe symptoms.*

*We ask all registries to report adverse events in donors that may be related to SARS-Cov-2 and also the so called 'risk of harm' reports that could involve donors who became SARS-Cov-2 positive during mobilization and did not seem to have experienced worse than expected symptoms.*

# Question 4

Q: Do you plan cargo flights for other destinations than US/Germany?

*A: Yes, Cargo “Care of Crew” or Cockpit solution can be extended to other countries. Both the registry that is shipping and the one that is receiving the product must be committed and set up a process for customs clearance.*
*If you need assistance with organising a flight or shipment, you can contact the WMDA Emergency Task Force: https://share.wmda.info/x/PqKbEw*

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# Thank you and stay safe!