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Improvement of the plasma collection and processing chain

Design of the product journey from collection to transport to fractionator

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I. Table of contents

II. Introduction

Blood establishments face plasma shortages and the challenges of acting. To fulfil European patients' need for plasma-derived medicinal products (PDMP), it is important that European Blood Establishment (hereafter BE) professionals work together to increase plasma collection in Europe. The SUPPLY project aims to increase and strengthen the resilience of plasma collection in the EU to enable a stable and adequate supply of PDMP in Europe. A significant part of the plasma collection in the EU is carried out by non-profit BEs relying on voluntary unpaid donors, however not at the required level. Part of the SUPPLY project therefore focuses on how BEs can improve and build voluntary unpaid plasma collection programmes and make them more efficient. Members of Working Package 3, Task 3.2 shared information, practices, and experiences to provide a report with recommendations to improve the plasma collection and processing chain and design optimal and more cost-efficient journey for donors, staff, and plasma from collection to transport to fractionator. (There may be subtle national (and regional) variations in the optimal chain).

The recommendations below take into account the current legislation and the EDQM guideline. It is anticipated that these recommendations will need to be assessed and potentially updated to align with any applicable changes made to the EDQM guidelines and/or the context of new legislation e.g. the proposed SoHo Regulation.

III. Description of the project

WP 3. Task 3.2 Description of the project task

Work Package 3 members represent 10 blood establishments from 10 EU Member States. Sanquin, the Netherlands, is the project leader for Task 3.2: Improving the plasma collection and processing chain: "Design of the product journey from collection to transport to fractionator". This project Task 3.2. has focused on the

following objectives of how blood establishments can improve the plasma collection and processing chain:

- The general objective of Supply Work Package 3 Task 3.2. is to provide a report with recommendations for good donor management practices to improve the plasma collection and processing chain and to design the product pathway from collection to transport to fractionator. This will help European blood collection professionals to ensure that good practices are applied at a local level.
- The most efficient and secure way to manage this chain is development and application of European good practices and cooperation between blood establishments and professionals at the European level.
- We will also provide effective methods to achieve a (cost) efficient collection to transport to fractionator process.

IV. Products and milestones

We have implemented the following milestones:

1. A survey on current practice in European blood establishments, including benchmark of best practices.

2. Development of a "plasma collection for transport to fractionator process" flowchart to identify and recommend good European plasma donor and product management practices.

3. Development of content for the SUPPLY platform with recommendations that will help blood establishments to develop an optimal plasma collection process within each EU Member State. These recommendations can also be useful to other European and extra-European countries.

V. Activities

The following blood establishments participated in the creation of this deliverable:

The Netherlands	Stichting Sanquin Bloedvoorziening
Belgium	Belgische Rode Kruis
Portugal	INSTITUTO PORTUGUES DO SANGUE E D TRANSPLANTACAO IP
Schotland	THE BLOOD TRANSFUSION SERVICE BOARD
Denmark	AARHUS UNIVERSITETSHOSPITAL
Germany	UNIVERSITAET HAMBURG
Slovenia	ZAVOD REPUBLIKE SLOVENIJE ZA TRANSFUZIJSKO MEDICINO
France	ETABLISSEMENT FRANCAIS DU SANG
Italy	ISTITUTO SUPERIORE DI SANITA

Spain	MINISTERIO DE SANIDAD

Workshops

Work Package 3 Task 3.2. members have organized 9 workshops to share the process information of their blood establishments. They also provided a comparison of the differences and similarities during the workshops. Two of the workshops took place during site visits in Denmark and Scotland. On the basis of these results, members have established standards and criteria to be used for the final recommendations.

During Task 3.2. project team members discussed differences and agreements of their practices in their respective Blood Establishments. Based on the first conclusions, a detailed journey "from collection to transport to fractionator" was drawn. These interim results served as a basis for discussion in special virtual workshops aimed at providing recommendations on each step in the production process: collection, processing, and transport to fractionator. Based on the results of the workshops during the site visit in Denmark, the flow chart was adjusted accordingly. Based on this first visit, an additional site visit was organised in Scotland to evaluate the flow chart in real conditions and another workshop was planned to discuss the results and prepare the final trip. The final flow chart (recommendations) includes a manual and a tool to support the BEs in implementing the recommendations. The recommendations will be disseminated to Blood Establishments (hereafter BEs) with plasma collection programmes and to countries without such programmes (WP7).

Survey

A survey (Chapter X References) was designed to identify bottlenecks of all steps in the EU members' processes that may hinder an optimal use of resources. This

survey was also used to benchmark management practices in European blood establishments, focusing on topics such as:

- what policies, routines, and procedures in the plasma chain are currently taking place?
- how do blood institutions deal with plasma topics such as:
    - donor registration
    - haemoglobin concentration and blood pressure measurement
    - tests for infectious markers
    - digitization
    - donation volume
    - MD presence in donor centres.

Strategies and procedures include methods within the plasma collection chain. In addition, issues related to plasma donor characteristics and the approval of plasma quality, safety, and availability were addressed, including how blood establishments address practices aimed at an effective chain.

The survey was designed on the basis of interviews during the workshops and on-site visits with participating members of Work Package 3 Task 3.2: Belgium, France, Denmark, Scotland, Germany, Slovenia, and the Netherlands. The subjects in the survey showed the current practices of blood establishments in the European Member States. The survey was then conveyed to the participants and discussed, after which it was completed.

Survey data collection / Benchmark BE partners

The survey was sent to SUPPLY participants and BEs in EBA member states. 40% of all surveys were completed and returned. Respondents could get help completing the survey by emailing or calling WP3 Task 3.2. project leader. The WP 3 team would then process all questionnaire data and create a data file to serve as input for the construction of this report. Within the working package Task 3.2 the survey data from the European partners (including Scotland) were analysed and the results

described (data analysis report). Based on these results, the Task 3.2 has established standards and criteria reflected in this report.

Site visits

With the members of WP task 3.2, two site visits (based on availability) were carried out to characterize the practical path from collection to transport to fractionator. During these visits, comparisons were made between how the different blood establishments comply with the regulations and requirements for collection, freezing, storage and transport conditions.

Odense Denmark

Odense Denmark Fig. 1

The donor centre in Odense is one of the five BEs in Denmark that all operate independently, although there is nationwide communication and cooperation. Each BE operates in one of the five country's regions and they are all part of the public hospital system. The donor centre in Odense is a permanent location where, in addition to plasma exchange procedures, plasma and platelets are collected. Besides this location the BE has three blood mobiles for whole blood, each with five beds and three other fixed sites for whole blood donation as well as two smaller plasma collection sites. The donor centre is open all year round (except for 5 bank holidays). The opening hours are: Mondays to Thursdays from 7.30 am to 8 pm, Fridays from 7.30 am to 5 pm. On Saturdays, Sundays and bank holidays: from 8 am to 5 pm or from 9 am to 6 pm.

Registration

For registration there are 6 kiosks with an electronic questionnaire. The donor goes directly to the kiosk upon arrival and fills in the questionnaire. This only takes a 2-4 minutes The donor identifies himself at the kiosk by means of the social security number and the finger code for verification (at the end of the questionnaire) and by

means of a signature. The donor is registered in the system. The donor takes something to drink and eat (cookies or crisps). There is no employee present to assist at the kiosks and there is no volunteer present. The electronic questionnaire is specific to plasmapheresis donors (e.g. malaria question not required) for women and men. e.g. no question about pregnancy in men). No Hb is measured, and no blood pressure is measured prior to donation. The Hb is determined afterwards from a tube once a year for plasma donors. If the Hb is too low, a flag is added to the donor record and the donor's Hb is determined via a tube (venipuncture) upon their first presentation for donation after the initial Hb result has been determined**.**

Health Examination

Health examinations are carried out in two rooms by two employees. If the donor is approved to donate, a queue number is printed and labels with information such as blood group and details for the collection and barcode labels used on the collection bags and tubes. First time donors can directly donate plasma. The donor's queue number is visible to the donor in the waiting area. At that moment, the waiting period for the donation begins. In the collection room there is a device that indicates the waiting time of a donor. The aim is that the waiting time for pick-up does not exceed 5 minutes. There is also a screen with various collection information.

Apheresis Collection Room

The Apheresis Collection room has 24 beds and 24 Nigale apheresis machines, from the firm Stradis-Med. A sealer is available with each bed. In Odense there are 22 donation beds and at least 3 employees working in the collection room per session. The goal is to perform 40,000 plasma pheresis per year by 2023.

There is no doctor on-site during the opening hours of the donor centre. Remotely there is 1 consultant for all collection locations (as well as hospitals treating patients with transfusions) that are open in the region who is accessible for consultation by phone. In the donor centre there is a call centre. The employees mail/text/call donors to the donor centre in Odense, one blood mobile and the smaller plasma centre in Svendborg – all together 55,000 plasma donations per year. This staff is also responsible for the interview process. They are 8.24 FTE covering the interview function in all the opening hours mentioned above.

Regarding traceability, data from the apheresis machines, all labels of bags and tubes, including lot no of consumables (bags, needle, citrate etc.) and staff are collected either directly (information from the machine) or by reading bar codes. The information is collated in software provided by Stradis-Med/Nigale and transferred by interface to the general Blood Establishment Computer System (ProSang, CSAM AB, Stockholm, Sweden).

Donors can donate up to 26 times a year. The donors do not receive any presents. During and immediately after pick up they get drinks and food. Different volumes are collected from plasmapheresis donors with regard to weight (weight 60-70 kg: 600 ml, weight > 70 kg: 700 ml and weight > 80 kg and male: 800 ml). No replacement fluid is returned.

Optimally, 1 plasmapheresis/bed/hour can be performed. An apheresis procedure takes approximately 60 minutes: counted from the moment the donor arrives until the

plasmapheresis unit is ready. The donor will be approx. 45 min on the bed. Currently, between 700 and 800 successful plasmapheresis procedures per week are performed.

In Odense a plasma set is used, where a few more handlings have to be performed before it can be installed on the plasmapheresis device. In this case an open system is used. In some countries, the plasma set can be installed directly on the plasmapheresis device. In this case, a closed system is used.

Required personnel (Overview)

In Denmark, there are no doctors present to oversee the entire donation process or for the medical examinations, there is all the time an "on call" doctor available. There are also no employees present at the reception, the registration area or the donor café. The employees take care for a short examination, collection, freezing/storage plasma products and call donors.

Recruitment

Recruitment of blood donors is (by the Danish blood law) the responsibility of the donor organisation. They have a central office in Copenhagen as well as local chapters around the country. The latter has a board of voluntary unpaid citizens that organize the recruitment.

A new donor does not have to donate whole blood during the first visit. New donors are not seen by a doctor during the first visit to the donor centre.

Electronic blood bank system

To work with Nigale and also in order to work wireless, bar code readers (Motorola) are used. Nigale is paired with Pro Sanq (CSAM AB, Stockholm, Sweden). Industrial, duplicated servers (IBM/LINUX) are used. They are placed in the region's IT-centre. All data from all donor centres (and information regarding patients and their transfusions) are stored in one regional database. In 2024 all data from the 5 blood centres will be stored in one national database run on servers in the Capital Region's

IT centre. The laptops used are Windows computers with ProSang installed are stored every 3 minutes. Printing reports is possible. A wireless bar code reader is available for every employee. The wireless bar code readers can be used for 8 hours. 2 batteries are required per PDA, otherwise you cannot work from 7 am to 8 pm. At the end of the session, the PDA goes into a charger.

Freezing and storage in donor centre Odense


photo 1


photo 2


photo 3


photo 4


photo 5

After collection the plasma units are placed directly on a trolley (photo 1). When full or at the end of the day this trolley is placed in a freezing cabinet (photo 2) where the plasma is frozen to a core temperature of < -25°C. After that the trolleys are placed in a freezing storage (< -20°C; photo 3). When test results are ready the units are released and packed in a room with a temperature of 5°C (photo 4). Afterwards the

plasmas in boxes are placed directly on pallets (< -20°C; photo 5), which are collected by the fractionator once a week.

This procedure means that there are only hands on the plasma units one time after collection.

2. Edinburgh, Scotland

The donor centre in Edinburgh is one of 6 donation centres in Scotland that operates as a part of the Scottish National Blood Transfusion Service within the National Health Service (NHS) Scotland. The donor centre in the centre of Edinburgh is a fixed location where whole blood, plasma and platelets are collected. The opening hours for the Edinburgh Donor Centre are: Mondays, Fridays and Saturdays from 10 am to 4 pm; Tuesdays, Wednesdays and Thursdays from 12 noon to 7 pm and are closed on Sundays.

Donor Registration

For registration, there is a desk with an employee who welcomes and identifies the donor and hands over the questionnaire. The donor is registered in the system. The donor takes a seat and fills in the questionnaire.

Donor Health Screening

Health examinations are carried out in 2 rooms by 2 employees. The printed DIN codes and the questionnaire are used during the Health examination within the Examination room. The Donor is called into the examination room for a Health screening. Answers to the questionnaire are personally reviewed and any queries addressed, potentially leading to referral to the Nurse, The Nurse can call on a Medical Team. Hb is measured, but no blood pressure is measured prior to donation. Any deferrals or comments are added to the Donor records in the system / donor database (eProgesa).

Whole blood and plasma collection

The collection room has 14 beds, 8 for whole blood and 6 for both plasma and platelet apheresis. A sealer is available with each bed. The Scottish National Blood Transfusion Service goal is to collect 10,000 plasmapheresis units across Scotland by March 2025. There is no doctor on site at the opening hours of the donor centre, however on-call Medical Team available. Donors can donate plasma up to 26 times a year. However, they receive donation recognition awards (certificate and badges). There are 2 employees present who call apheresis donors only for an appointment. There is no software system that can automatically read plasmapheresis data. Different volumes have been taken from plasmapheresis donors by height and weight criteria. No compensation fluid will be returned. All employees are qualified to work in the Health screening, donation suite, administration areas. Whole blood and plasma are transported in unrefrigerated portable boxes to the central processing site near Edinburgh city centre.

Workshops were also organised during both site visits in Odense and Edinburgh. With regard to the plasma collection to processing chain, it was discussed which aspects apply to the design for an optimal plasma collection to processing process. In addition to regulations and guidelines from the EDQM Guide and EU Blood Directive, national legislation and derivatives also influence the plasma collection process.

The following topics were discussed for conclusions and recommendations:

- Interpretation and use; differences in interpretation of the EDQM Blood Guide;
- Haemoglobin and blood pressure measurement;
- Responsibility during opening hours at the donor centre: no presence of doctor during examination and collection, only qualified employees;
- Donor Home check to prevent collection-free visit;
- Maximum plasma donation frequency per year;
- Plasma collection in bottles/vials or bags?
- Volume: differences in plasma efficiency: calculation in litres in addition to kilograms;

- Digitization: bidirectional connection, automatic integration of collection administration → blood bank/collection management system;
- Cooling and freezing infrastructure (in/out of the plasma centre);
- Maintaining an ambient temperature of 20-25°C for plasma and whole blood products during on-site collection and transport;
- Refreshment policy;
- Performance monitoring (screens)/KPI/Performance monitoring system (targets/volumes);

(See Chapter VII conclusions and VIII recommendations and further steps).

VI. Design of the product journey

Image board 'From collection to transport to fractionator'

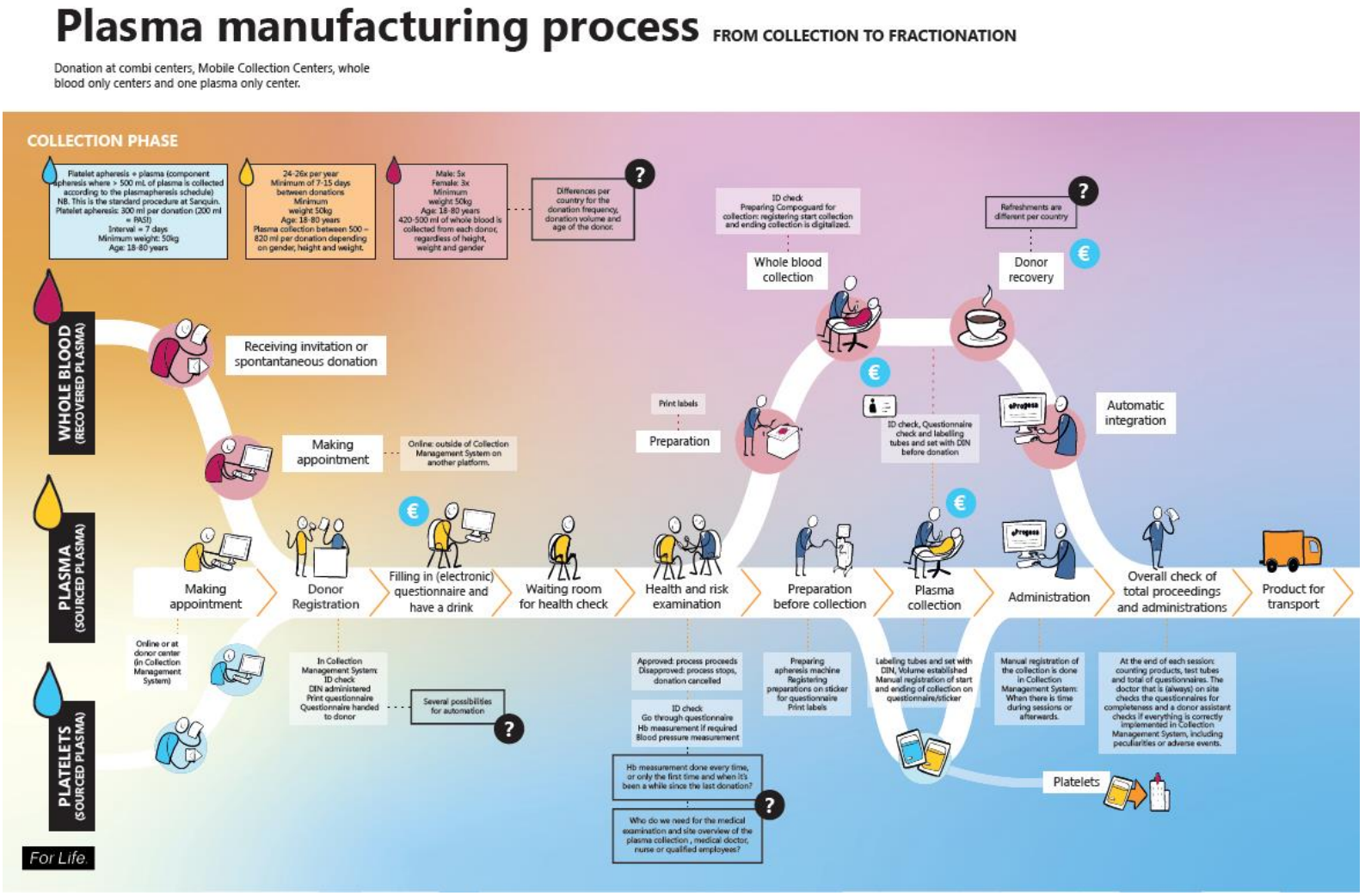
Many milestones mark the journey of source and recovered plasma, from the collection through apheresis, through processing and transport to fractionator. The product journey of the plasma process and the individual steps are visualized in two phases:

- the collection phase: from donor registration to collection;
- the processing and transport phase: from collection to distribution to fractionator.

An inventory is made of all steps for an optimal production process from collection to transport for fractionation. On the next page, the image boards of both phases are shown and each process step is described/illustrated. The process was roughly visualized, after which the participants commented on the visuals. These changes have been discussed with the relevant participants and included in the next version of the image board. During the workshop in Scotland, the last comments were added and the final image board was realized.

The full (readable) image board is attached to this report (see Chapter VIII Appendices).

Collection phase - image board 1



<u>Step 1: Make an appointment</u>

Donors (whole blood, plasma or platelets) receive an (online) invitation to make an appointment (date and time) for donation or make an appointment by themselves. Plasma donors are usually loyal donors and may be encouraged to schedule appointments in advance, for example, by asking staff to schedule a new appointment for the donor on site before leaving the donor centre or by website booking,

Recommendation:

Making an appointment immediately after donation is key to keeping the plasma process and the donor pool running. A website provides a donor monitoring module to prevent a donation-free visit to the donor centre. It also provides easy access to an appointment schedule where the donor can choose a date with a favourite time slot. An online real-time schedule helps donors anticipate how busy the donor centre will be that day.

Step 2: Donor registration

When the donor arrives at the donor centre, the donor must provide proof of identity (name and date of birth are checked) and is then registered. The donation type is determined, the Donation Identification Number (DIN) is administered and the donor is given the correct questionnaire to complete.

Step 3: Fill in the questionnaire and have a drink

The donor completes the questionnaire (electronically), while drinking 300 ml of water before the donation. The questionnaire is handed over to an employee or processed digitally.

Recommendation

The questionnaire should be digitalised. It is possible to fill this in at the location by means of an iPad or similar, In Denmark a column with an iPad is used for this.

Drinking before and after plasma donation is key.

Step 4: Waiting room for health check

The donor waits in the waiting room until called upon for the health check.

Step 5: Health and risk examination

The health and risk examination takes place in a separate examination room. Blood pressure and Hb are determined. Deviations from the questionnaire are discussed. All this will determine whether the donor is fit and healthy enough to donate.

Recommendation

It is not strictly necessary to perform a Hb measurement or blood pressure measurement. Consideration should be given to omitting them, unless at the start of a donor career Hb measurement should be performed. This could be after a plasma donation.

It should be possible to donate plasma directly during a first visit. It must be taken into account that this donation must be quarantined until the donor has donated a second time.

Step 6: Preparation for pickup

If all is well, the donor goes to the collection room. Name and date of birth will be checked again. The donor is asked if the left or right arm is preferred for venepuncture and is led to a collection chair. In the meantime, an employee is preparing the collection system. Plasma is collected in three ways: by plasmapheresis, by platelet donation, or is derived from whole blood donations.

Recommendation

It should be considered to allow the donor to move independently through a location. An automatic queuing system or hostess could be an option.

Step 7: Plasma/Whole Blood/Platelet Collection

The venipuncture is performed and the donation process begins. After donation, aftercare is provided and the donor is thanked for his donation. All donors will be offered a drink (and snack) before departure.

Recommendation

It can be considered to base the volume of donation to be collected solely on body weight (see above at "Odense Danmark").That can provide the advantage to give clear limited categories to determine the plasma collection volume.

Step 8: Administration

After the collection procedure has been completed, the administrative procedure is mostly carried out manually in a digitalised BE system. The integration will be fully automatic (i.e. the machine is linked to the BE management system). In Denmark, Sweden, Iceland, Latvia and 2/3 of Norway ProSang is used. Belgium's Red Cross Flanders uses Edge by Inlog. In the other countries eProgesa from MAK systems is used.

Recommendation

There must be a bi-directional connection between the apheresis device and the BE system. This eliminates the need to manually transfer data to the BE system.

Step 9: General control of the entire procedure and administration

At the end of the session, all products, test tubes and questionnaires are counted if not accounted for by a digital process. The doctor checks whether all questionnaires have been completed correctly; an employee checks the entry into the Collection Management System.

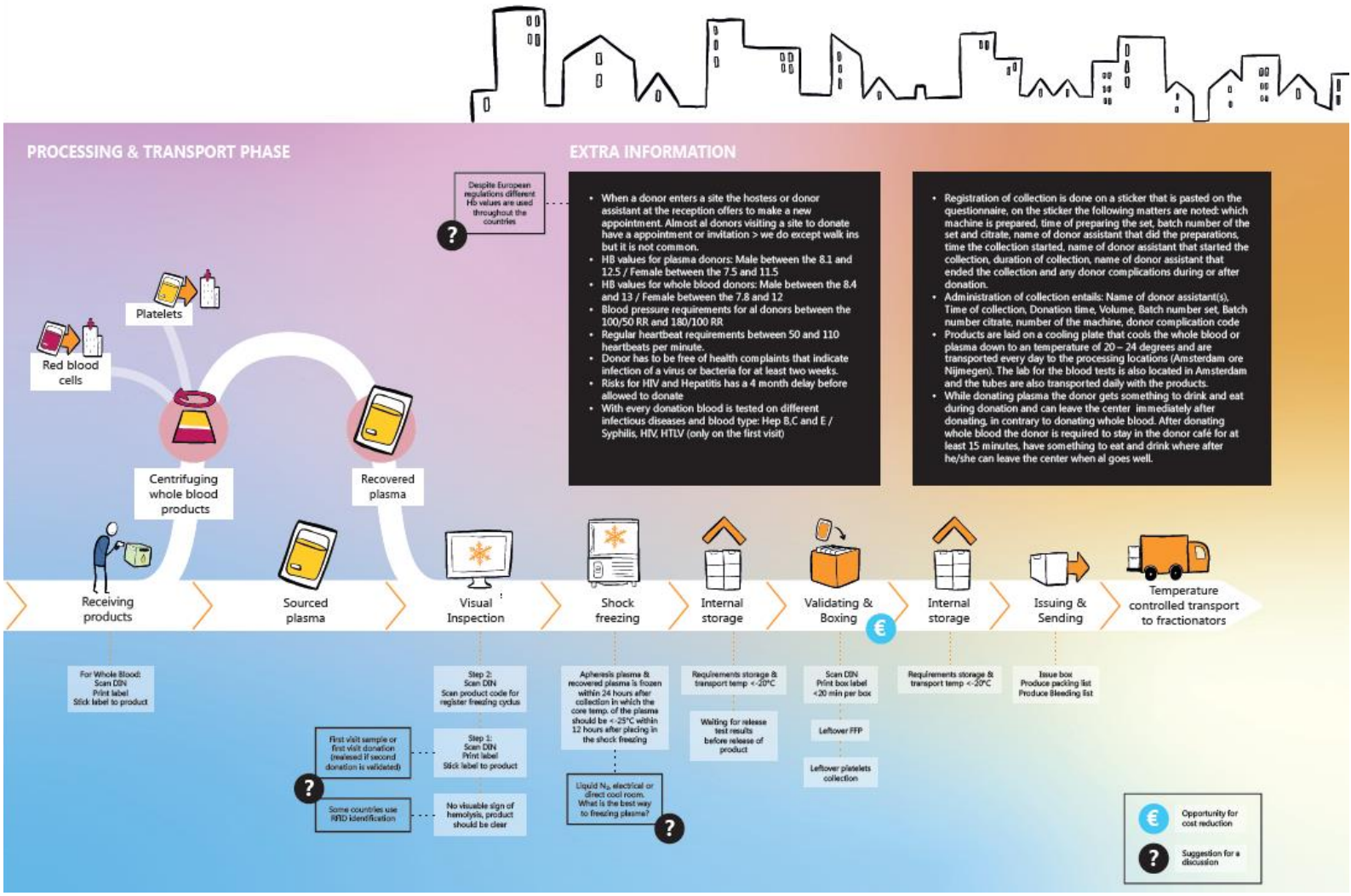
Recommendation

See previous recommendations about digitalisation. If all processes are automated, checks do not have to be carried out.

Step 10: Storage product before transport or processing

Now all collected blood products are ready for transport and are stored accordingly: tubes in test tube racks; whole blood collection bags are placed on cooling plates, put in climate cabinets or in climate containers to reduce the temperature to 20°C - 24°C.

Processing and transport phase - image board 2



Step 11 Processing of donations

The donations arrive at the processing sites, which can be located in the same building as the donor centre or at a different location (i.e. transport by truck). Whole blood will be processed and separated into 3 components, namely red blood cells, platelets and plasma or into 2 components, namely red blood cells and plasma. Of course, this step is not necessary for sourced plasma. Among the respondents to the survey currently plasmapheresis is used in Denmark, Sweden, United Kingdom and Italy, France, Belgium, the Netherlands, Germany, the Czech Republic, Hungary and Austria.

Recommendation

Try to keep the plasma collection process as simple as possible. Virus inactivation is only necessary if the donated plasma is used as Fresh Frozen plasma.

Step 12: Visual inspection

The product should be clear, free from haemolysis. The barcode (DIN) is then scanned, a label is printed and attached to the donation/bag/Units. The barcode (DIN) is scanned again to record the freezing cycle.

Step 13: Shock freezing

Plasma should be frozen soon after collection. The faster it is frozen, the more the essential labile proteins are preserved. Apheresis and whole blood plasma are frozen within 24 hours of collection, with a core temperature of < -25°C established within 12 hours of placement in the freezer (EU Guide or rather the European Pharmacopoeia (Ph. Eur.) monograph “Human Plasma for fractionation” (0853)). For source plasma this freezing procedure can be carried out at the processing sites or at the donor centre.

Different techniques can be used for freezing plasma. The most commonly used method is the use of a "blast freezer" or freezing by using nitrogen.

Recommendation

A freezing and storage temperature of -25°C is recommended. Try to carry out the freezing process as soon as possible, to protect proteins as well as possible.

Step 14: Internal storage

Only after the release of the test results can the donations be released. Until then,

the product is stored internally at ≦ -25°C.

Step 15: Validate & Box

Plasma units are packaged: after scanning the DIN, a box label is printed. This step is time-consuming (20 minutes per box) and is therefore an interesting topic for cost reduction.

Recommendation:

Boxing and release of products have to be done in one step and should be completely paperless.

Step 16: Internal storage

The products are transported and stored at room temperature (≤ 25°Celsius).

Step 17: Issuance and shipping

A packing list for products / donation / Units is sent along with the distribution box.

Step 18: Temperature-controlled transport to fractionators

Temperature controlled transport (using climate boxes, temperature conditioned vehicles, e.g.) is used to transport the products to fractionator or hospital in case of virus inactivated plasma.

VII, Conclusion

During this project Task 3.2. was looking for an answer to the question: "How to improve the plasma collection and processing chain; Design the optimal product journey from collection to transport to fractionator”. This goal was carried out in BE's current site visits and discussed in meetings about their effects on the plasma journey.

In the development of the optimal plasma journey, a number of differences between the countries are apparent, namely:

- the origin of the plasma is different. In most countries, plasma is obtained as recovered plasma from a whole blood donation or as an additional plasma donation during a platelet apheresis procedure. The plasma apheresis procedure has not yet been introduced in all countries. As a result, the plasma yield in such countries remains low. Introduction of plasma apheresis is necessary to increase the yield of plasma.
- There is a lack of consensus in the implementation of the EDQM guidelines. Examples include:
    - the limit values used for Hb and blood pressure. For this reason, an interval is included in the plasma journey within which the different values fall. The intervals for the Hb measurement are between 8.1 and 12.5 for a man, while for a woman this is between 7.5 and 11.5. For blood pressure, it is between 100/50 and 180/100.
    - in some countries there is no Hb measurement or an Hb measurement with an interval, which seems to be the same for measuring blood pressure.
    - the plasma volume to be taken has not been determined unequivocally. This ranges from 500 to 820 ml per donation. In a number of countries categories are used, in other countries the volume is calculated on the basis of body weight and height of the donor.
    - there is no consensus regarding how often a donor may donate, this varies from two times a week to less.

Consideration should be given to see the EDQM guidelines as a directive and not as recommendations. This is as currently envisioned in the proposed SoHO Regulation.

- In some countries, during a first visit of a new donor, only a medical examination with accompanying blood tests is carried out, in a number of countries this is also accompanied by a first donation of plasma that is then quarantined until the donor's next visit.
- The role of the doctor varies from country to country, and it seems that underlying legislation determines this. Donating and (medical) intake in that case is seen as a medical act that must take place under the supervision of a doctor. The following different systems are seen:
    - There is no doctor present during the sessions, but there is a doctor "remotely" present, who can be consulted during a session.
    - A doctor is present during the session, with the doctor only taking care of part of the examination. Regular examinations and are often carried out by employees who are not doctors. It is observed that this can be a nurse or non-medical staff.
    - A doctor is present during the session who takes care of all the examinations. It is not permitted for an inspection to be carried out by another person.
- The ferritin measurement is still in its infancy. Only in a small number of countries is the ferritin measurement carried out and on the basis of the ferritin value the donor is rejected and given a deferred term. A ferritin measurement is only necessary for whole blood donation, not advised for plasma apheresis (according to EDQM Blood guide)
- Ddigitization has not yet been implemented equally everywhere. Examples include:
    - the link via a bi-directional connection to the "collection management system" (called hereafter CMS) has not yet been realized everywhere. As a result, data is entered manually during the procedure. It seems

that countries that work with the MAK system are the most lagging behind.
    - of the participating countries, only 1 country works with a digital medical questionnaire, which is automatically passed on to the employee or doctor responsible for the donor's medical examination.
    - The entire process will be greatly improved and optimized if digitization can be introduced. This applies to the intake, the completion of the medical questionnaire, the transfer of technical donation data to the BE system and the release and boxes of the products.
- The testing of plasma seems to be fairly similar between the different countries. Often the testing is linked to the tests for whole blood, where it is particularly necessary to test for Hep B, C, Syphilis, HIV and HTLV.
- The transport of donated plasma from a collection site to a processing site shows differences. These differences are:
    - Donated plasma is frozen immediately after collection, no transport is necessary to a processing location.
    - Donated plasma is transported via controlled temperature transport (20-24°C) to a processing location.
    - Donated plasma is "packaged" for transport, so that the temperature fluctuates less during transport.
- The freezing of plasma shows few noticeable differences. EU countries freeze their plasma within the recommended time after donation. This is done either with a blast freezer, or by means of nitrogen. This explains the length of time it takes to freeze the plasma to a temperature of -30°C. However, it is seen that the temperature is part of the discussion, whereby it is now seen that plasma is frozen to a temperature of -25°C and can be recommended. The main motivation for this is that less energy is required and it has not been demonstrated why this is -30 or -25°C.

VIII. Recommendations and further steps

The same general process is used in most countries, with (slight) differences here and there. In itself, this is strange because all countries work with the same EDQM guideline. Sometimes it concerns a difference due to BE's interpretation, sometimes due to an underlying national legislation.

It is advisable to further examine the main differences with a high economic value or to introduce them in the short term. Our recommendations for all European BEs to reach a certain uniformity are:

1. Automate and digitalise processes. In many countries, there are still insufficient automated and digitalised processes. The greatest benefits can be achieved if the processes are optimally digitalised and paperless. For example: implement electronic donor questionnaires.
2. Look for a way to make sure the EDQM Guideline is interpreted the same way in all European BEs. Find out, for example which role a doctor or nurse should play during the plasma donation. Is the presence of a doctor or nurse always necessary and see what is possible from the point of view of underlying legislation.
3. For plasma, perform the following viral tests: Hep B and C, Syphilis, HIV and HTLV. Establish a bi-directional connection (through suppliers of apheresis devices or CMS) in order to create a direct communication link with the donor database.
4. Ferritin measurements should be limited for whole blood donation and not introduced in plasma apheresis. This can lead to unnecessary delays for donors.
5. Further research is needed to determine whether it is necessary to take an Hb measurement or blood pressure measurement is necessary for a plasma donation.
6. Donation frequency for plasma donors in all countries should be the same. Further research should show what is possible in this, also in relation to,

for example, the influence of donation frequency on the protein content in plasma.

7. Plasma donation volumes based on weight. Always measured in litres instead of kilos.

IX Attachments

Image boards:

- Collection phase;
- Processing and transport phase;
- Complete plasma collection to transport to fractionator process.

X. References

1. From the "Deliverable SUPPLY Time Table"

D3.2 : Recommendations on plasma manufacturing journey

SQ 21/08/2023 31/08/2023

2. Survey: WP 3 SUPPLY SURVEY Cost modelling / Plasma process