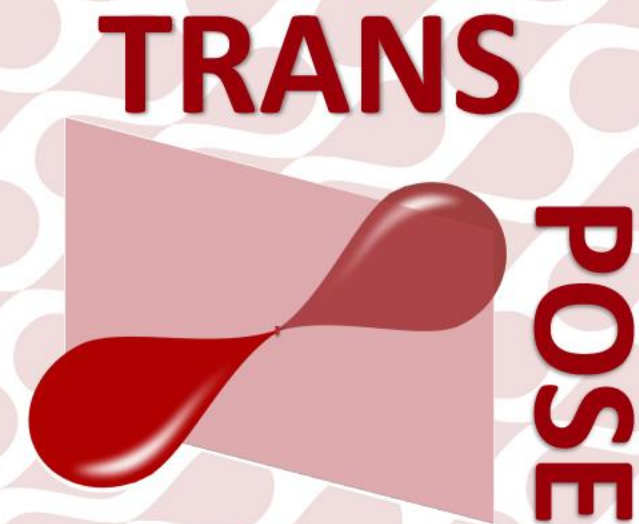




Grant Agreement 738145

TRANSfusion and transplantation PrOtection and SElection of donors



Co-funded by
the Health Programme
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TRANSPOSE

*(TRANSfusion and transplantation: PrOtection
and SElection of donors)*

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TRANSPOSE Project Leader

Sanquin Blood Supply

The Netherlands

bioef

berrikuntza + ikerketa + osasuna eusko fundazioa
fundación vasca de innovación e investigación sanitarias



**Region
Hovedstaden**



**BANC DE SANG
I TEIXITS**



Sanquin
Blood Supply



ÉTABLISSEMENT FRANÇAIS DU SANG

Blutspendedienst
des Bayerischen Roten Kreuzes



NHS

Blood and Transplant



**UNIVERSITY OF
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Aarhus Universitetshospital



Regionaalhaigla



CSL Plasma

Punainen Risti

health.gov.mt



Zavod Republike Slovenije
za transfuzijsko medicino

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SANGUE**



Universität Hamburg
DER FORSCHUNG | DER LEHRE | DER BILDUNG



**IP
ST**

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Transplantação, IP**



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27/05/2019

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TRANSPOSE aims at a structured, alternative approach to construct risk-based Guidelines and a standard DHQ for the procedures used to collect SoHO, including the selection and protection of donors.

The objective of this action is:

- To collect and compare EU and national ***donor selection and protection criteria***;
- To identify the information needed from donors or their families to allow the application of ***appropriate donor deferral or exclusion criteria for the protection of recipients***; and
- To propose ***approaches to control and minimise these risks***.

Work Packages

There are three horizontal work-packages (WPs);

- Coordinating,
- Disseminating, and
- Evaluating the project.

Four **technical** ones with specific deliverables and milestones to be regularly produced, according to the Grant Agreement.

WP Number	WP Title	Lead Beneficiary
WP1	Coordination of TRANSPOSE	Sanquin Blood Supply
WP2	Dissemination of the results of TRANSPOSE	Centro Nazionale Sangue
WP3	Evaluation of TRANSPOSE	Établissement Français du Sang
WP4	Inventory of Donor Selection & Protection Practices	University of Cambridge
WP5	Development of Donor Selection & Protection Guidelines	Region Hovedstaden Denmark
WP6	Development of a Standard Donor Health Questionnaire	University of Hamburg
WP7	Training Course/Workshop on the Use of the Guiding Principles	Sanquin & Centro Nazionale Sangue

WP2 (Centro Nazionale Sangue)

Dissemination of the Project:



Forum	Topics	Posts	Freshness
General discussion	2	2	3 months, 2 weeks ago Donata Forliso
WP Leader	1	4	2 weeks, 1 day ago Sabrina Sandhor
WP1	0	0	No Topics admin
WP2	0	0	No Topics
WP3	0	0	No Topics
WP4	1	1	1 year ago Lars Eberhart
WP5	1	2	1 week, 1 day ago Christina Mikkelsen
WP6	1	7	1 week, 1 day ago Eva-Maria Morz

<https://www.transposeproject.eu>

News

December 31, 2018



Grant Agreement 738145
**TRANSfusion and transplantation
PrOtection and SElection of donors**

Published by  Marcella Lembo

Newsletter 2: TRANSPOSE state of the art

The second newsletter is now available on the Download Area of the website.

[Read more](#)

July 25, 2018



Grant Agreement 738145
**TRANSfusion and transplantation
PrOtection and SElection of donors**

Published by  Marcella Lembo

**TRANSPOSE
Newsletter 01**

The newsletter is now available

The first newsletter is now available on the Download Area of the website.

[Read more](#)

December 18, 2017



Published by  admin

Over 5 million patients in EU depends on donors, a project to harmonize selection and protection

Over 5 million patients in the EU annually receive transfusions or transplantations of substances of human origin (SoHO): blood components, plasma-derived products, tissues & stem cells, [...]

[Read more](#)

November 24, 2017



Published by  admin

The leaflet is now available

The leaflet of the Transpose Project is available in the download area of the website.

[Read more](#)

WP4 (University of Cambridge)

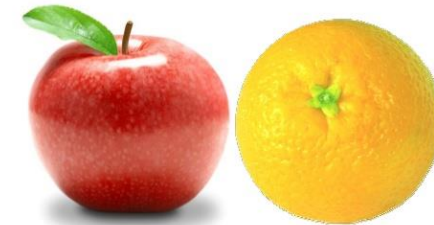
Inventory of Donor Selection & Protection Practices

Leader: Emanuele di Angelantonio (University of Cambridge)

- Surveys were sent to experts about current practices donor selection and protection (all SoHO)
- In-depth inventory (interviews) of current practices of donor selection and protection
- Overview of similarities and differences

Completed

**IDENTIFYING
SIMILARITIES & DIFFERENCES**



WP4 - Inventory of Donor Selection & Protection Practices

- In-depth semi-structured interviews with key stakeholders in all SoHO:
 - identify main topics for improvement of current donor selection criteria (DSC)
- Results:
 - DSC are perceived redundant on a substantial number of aspects
 - Many regulations could be improved to diminish deferrals and decrease donor risks.
 - TRANSPOSE will add to reviewing, improving and harmonizing these regulations and criteria.
 - TRANSPOSE will provide suggestions to improve directives and guidelines and a DHQ (both donor health protection and safety of donations), but also removing deferral criteria that are not relevant (anymore), and offer a future research agenda to make DSC more evidence-based.

WP4 – Survey Results

- Survey was sent to professionals from collection institutions of all SoHO
 - to get feedback from as many EU-MS organizations as possible (n=163)
 - 40 blood; 40 plasma; 27 tissues; 47 stem cells; 9 ART and 39 (24%) completed questionnaires
 - where information was lacking, additional experts were asked to recommend upon DSC.

WP5 Development of Donor Selection & Protection Guidelines

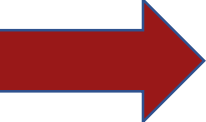
Leader: Henrik Ullum (regio Hovedstaten Denmark)

- Critically reviewing risks both donors and recipients (scientific paper) (June 2018)
- Assess those risks in a workshop to produce guiding principles on eligibility criteria (October 2018)
- Finalise risk-based donor selection and protection criteria in a workshop (April 2019)
- Final guiding principles for critical evaluation of existing donor eligibility criteria and development and validation of emerging eligibility criteria (June 2019)



WP5 - Development of Donor Selection & Protection Guidelines

Outcome:

- Diverging opinions across members on certain criteria and a wide lack of evidence.
- We re-assessed all items in the current criteria in order to propose expert-based or evidence-based recommendations: namely the Donor Selection & Protection Guidelines.
-  Risk assessment method, used per risk for all SoHO
- TRANSPOSE meeting of April 2019: start writing up the Guidelines which will be submitted as a scientific paper.

The TRANSPOSE Risk based assessment approach was partly based on the Risk-Based Decision-Making Framework - Alliance of Blood Operators)



The Risk-Based Decision-Making Framework was developed on a four-part foundation, building out of:

- a series of Risk Management Principles stating what must be observed in making decisions about risk;
- a communications and consultation policy describing expectations for the consultation and education of stakeholder groups and of the general public;
- a set of Risk Tolerability Criteria defining when a risk can be deemed acceptable in light of the benefits gained; and
- a policy for conduct of natural and social science assessments, including economic and social concern assessments, to ensure that they serve as credible inputs to risk management decisions.

Tissue Risks

- Bacterial/fungal transmission
- Graft failure
- Malignancies
- Viral infections

a. What the issues are;

- Risk of Bacterial/Fungal infection transmission through tissue donations - there are several reports of either definite or probable transmission of both bacterial and fungal infections either of donor source or due to possible contamination during processing from a range of tissue donations, including adipose tissue donations, bone, heart valves, tendons and especially (i.e. most common) cornea donations.
- Some tissues like cornea, sclera and epidermis are per definition populated with bacteria and even fungi. In deceased donors for instance bacteria are also expected to be present on the ocular surface due to lack of blinking and tear film
- It is important to remember that a diagnosis of systemic bacterial infection at the time of donation is not necessarily considered a reason to defer a donor when there is no indication that the procured tissue comes in contact with the infected substance. In cornea donation for instance sepsis has not shown to infect the cornea tissue or lead to infection of the recipient with the septic bacteria when corneas are stored in organ culture¹, while the presence of any systemic infection would lead to the donor being deferred from heart valve/tendon donation
- Issues related to (select all that apply): ☐ donor ☒ recipient
- Severity

grade of severity*				
Risk(s)	Non-Severe	Severe	Life-threatening	Death
			x	

Due to the transmission of bacterial/fungal infection there are reports of recipients losing their eyesight or requiring re-do heart valve surgery or orthopaedic surgery in some cases requiring prolonged antibiotic treatment and occasionally contributing to the patient's death - refer to Notify library for detail.

- Imputability

level of imputability*						
Risk(s)	Definite/Certain	Likely/ Probable	Possible	Unlikely	Excluded	Not assessable
	x					

¹ 1: Chu HS, Lai CT, Hou YC, Liu HY, Wang U, Chen WL, Shih CL, Hu FR. Reappraisal of the suitability of corneas from bacteremic donors for use in corneal transplants. Br J Ophthalmol. 2018 Oct 15. pii: bjophthalmol-2018-312816.

2: Spelsberg H, Reinhard T, Sengler U, Daeubener W, Sundmacher R. Organ-cultured corneal grafts from septic donors: a retrospective study. Eye (Lond). 2002 Sep;16(5):622-7.

It is worth noting, imputability in relation to the source of infection in post corneal transplant keratitis/endophthalmitis can be difficult to establish. Beside contamination during transplantation the limited time available to culture corneas before distribution may not reveal the presence of slow growing bacteria and certain fungi.

• Options to minimise each of the risks

1. donor selection criteria - continue to defer potential tissue donors in the presence of untreated systemic infection or local infection affecting the tissue to be donated at the time of donation
2. identify which types/severity of infection present at the time of donation should lead to cornea donor deferral, based on storage method and sensitivity of microbiology screening
3. Organ-cultured corneas are currently accepted in the presence of most bacterial infections in the donor including systemic bacterial infections at the time of death, based on the fact that the donated corneas are kept in organ culture which contains a cocktail of antibiotic and antifungal agents with the aim of minimising the risk of microbial growth, and where present identifying it - ensure validated culturing techniques of sufficient sensitivity to detect the presence of clinically significant contaminants
4. Appropriate cleaning of the eyes prior to processing and application of aseptic technique are important
5. Ensure adequate validated culturing techniques to look for the presence of potential contamination (donor derived) - ensure sufficient samples are taken at key points in the retrieval/processing process and that the culturing techniques used are such as to identify all clinically significant contaminants i.e. ensure use culture media that support growth of aerobes, anaerobes and fungal and culture for long enough to identify slow growing organisms.
6. Consider risk of transmission of Mycobacteria e.g. tuberculosis - this will require specific culturing techniques.
7. Carry out validated decontamination of tissue in particular for donations that cannot be terminally sterilised
8. Consider terminally sterilising any donations that can be sterilised without compromising graft function.
9. In case of positive culture results becoming available post issue of tissue: Initiate recall if possible, and otherwise inform surgeon if tissue has already been transplanted, to allow adaptation of patient management as required
10. The Tissue bank must be informed within a set timeframe of an infection-related SAER to enable the tissue bank to investigate and avert harm from other recipients

b. Recommendations;

- Refer to section above re options to minimise the risks of transmitting bacterial/fungal infection

c. Justification (data/references);

- There are several reports (Notify Library) of definite or probable transmission of bacterial and/or fungal contamination through a range of tissue donations.

d. Considerations (e.g., financials, etc.).

- The validated outcome of decontamination/sterilization process determines the consecutive measures to be taken to render the tissue safe for recipients. However,

Plasma collection risks addressed in risk assessments

Donor risks:

- Low total protein and IgG,
- Low Hb and ferritin
- Relative overdraw of small/obese donors
- Serious donor reactions (vasovagal, hematomas, nerve lesion etc.)
- Repetitive exposure to large amounts of citrate (bone demineralization)
- Repetitive exposure to plasticizers (DHEP)
- Machine errors

Recipient risks:

- Infections of plasma with (so far unknown) agents
- (Teratogenic) medication

WP6 Development of a standard Donor Health Questionnaire

Leader: Michel Clement (University of Hamburg)

- Draft of first version of a standard donor health questionnaire (February 2019)
- Validated draft version of a standard DHQ (April 2019)
- Availability of standard DHQ and modules in principle languages



WP6 - Development of a standard Donor Health Questionnaire

Development of questionnaire is defined by several steps:

- Ask experts what is currently lacking (done via WP4 questionnaire)
- Develop the standard Questionnaire:
 - Database of basic questions which must be asked:
 - 1. General module (common trunk)
 - 2. Country & SoHO specific questions (customization)
 - How different risks should be assessed through different types of questions?
 - Decide between paired vs. individual risk assessment?

First-time donors

	General DHQ	DHQ Blood	DHQ ART	DHQ <u>Tissues</u>	DHQ Plasma	DHQ <u>Stem Cells</u>	
for all living donors						Registration	Donation
1. General							
1.1 Did you read the documents/information you received before?	x						
1.2 Have you eaten and drunk today?		x			x		
1.3 Do you weigh a minimum of 50kg?		x			x		
1.4 <u>Were you adopted?</u>			x			x	x
1.5 Were you conceived by donation?			x				
2. Health							
2.1 Are you healthy?	x						
2.2 Have you been hospitalized, consult a healthcare professional or have you had an illness (such as fever and diarrhea, heart and vascular disease or neurological diseases)?		x	x	x	x		
2.3 Have you visit a dentist in the last week?		x			x		
2.4 Have you had an uncomplicated infection?		x	x	x	x		
2.5 Do you have a chronic disease (e.g. allergies, diabetes) or a chronic auto-immune disease (e.g. <u>Crohns</u> , Graves, Lupus)?	x						
2.6 Are you using any prescribed or over the counter medication?		x	x	x	x		x
2.7 Have you had any <u>immunisations</u> or vaccinations in the last 4 weeks?		x	x	x	x		x
2.8 Have any of your close relatives been diagnosed with or have you been told you are at risk of Creutzfeldt-Jakob disease (CJD)?	x						
2.9 Before 1986, have you been treated with hormones of the pituitary gland, e.g. because of growth disturbance, infertility, endometriosis?		x	x	x	x	x	
2.10 Have you had an allergic reaction to general or local anesthesia?			x				x
2.11 Are you scheduled to be hospitalized or to have surgery?			x	x			x

WP7 - Training the use of Donor Selection & Protection Guidelines

Leader: Sanquin and CNS

(I) History & Introduction

- History, Eligibility, Precautionary principle, Current practices

(II) General Principles

- Importance donor selection and protection
- Ethics

(III) SoHOs

- Common risks and SoHO specific risks (how they're assessed)
- Risk mitigation (DHQ), 'toolbox' of questions

WP3 (Établissement Français du Sang)

Evaluation of the Project

September 2018, surveys were sent to 80 stakeholders; response: 22 (28%)

Recommendations:

- Verify adequate resource allocation for SoHOs other than blood
- Increase communication between project members (in particular between WP leaders and WP members) Increase the use of the TRANSPOSE website to share information
- More F2F meetings
- Better sharing information between WP leaders, EU and EDQM



Focus on Donor Protection

- Current focus on donor selection and protection:
 - Our take is that donor protection should begin from the start – thus we propose a more in-depth risk assessment method from the beginning and starting with new donors.
 - Furthermore, inventory of yet unknown/ theoretical risks for donors and those risks that have not been properly investigated.
 - Also a more harmonised risk based assessment method. To develop this, we have modified and simplified the ABO tool that is developed for risk assessment.

Next Steps

- Validation of the Donor Health Questionnaire (WP 6)
- Development of the Donor Selection & Protection Guidelines (WP 5)
- Start with DHQ and education and dissemination (WP 7)
- 3 presentations and 1 poster on TRANSPOSE will be present at the ISBT Conference in Basel (results of WP 4 and WP5).



Thank you for your attention!

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