



# Transplantation and Transfusion

*Projects and Actions for saving and improving the quality of life of citizens by facilitating transplantation and blood transfusion in the European Union*

Executive Agency  
for Health and  
Consumers



## Acknowledgements

This publication is the result of the joint work of Martina Melis (Cagliari, Italy), Jesús López Alcalde (Madrid, Spain) and Csilla Kaposvári (Strasbourg, France).

Comments, interviews and further material were provided by the project coordinators and project members of the respective projects and activities.

Comments were provided by the 'Substances of human origin' team of the Directorate-General for Health and Consumers of the European Commission.

Europe Direct is a service to help you find answers  
to your questions about the European Union.

Freephone number (\*):  
00 800 6 7 8 9 10 11

(\*) Certain mobile telephone operators do not allow access to 00 800 numbers or these calls may be billed.

### 'Monolith' by Cornelia Brandstetter

A pair in tight embracement. They are almost a monolith, mutually understanding and accepting each other's plight; donating an organ, giving life.

Giving in this manner transforms the world to hopeful green, the atmosphere to life-giving air. The sensitive use of colour gives this picture strong emotional power.

The views expressed in the report do not necessarily reflect the opinion of the European Commission and are not binding.

Neither the Commission nor any person acting on the Commission's behalf may be held responsible for the use which may be made of the information contained therein.

Online information about the European Union in 23 languages is available at:  
<http://ec.europa.eu>

Further information on the Directorate-General for Health and Consumers is available at:  
[http://ec.europa.eu/dgs/health\\_consumer/index\\_en.htm](http://ec.europa.eu/dgs/health_consumer/index_en.htm)

Information on the Executive Agency for Health and Consumers (EAHC) is available at:  
<http://ec.europa.eu/eahc>

Cataloguing data can be found at the end of this publication.

Luxembourg: Publications Office of the European Union, 2013

ISBN 978-92-9200-020-2  
doi:10.2818/14909

© European Union, 2013  
Reproduction is authorised provided the source is acknowledged.

Printed in Luxembourg  
PRINTED ON ELEMENTAL CHLORINE-FREE BLEACHED PAPER (ECF)

## HOW TO OBTAIN EU PUBLICATIONS

### Free publications:

- via EU Bookshop (<http://bookshop.europa.eu>);
- at the European Union's representations or delegations. You can obtain their contact details on the Internet (<http://ec.europa.eu>) or by sending a fax to +352 2929-42758.

### Priced publications:

- via EU Bookshop (<http://bookshop.europa.eu>).

### Priced subscriptions (e.g. annual series of the *Official Journal of the European Union* and reports of cases before the Court of Justice of the European Union):

- via one of the sales agents of the Publications Office of the European Union ([http://publications.europa.eu/others/agents/index\\_en.htm](http://publications.europa.eu/others/agents/index_en.htm)).

# Transplantation and Transfusion

*Projects and Actions for saving  
and improving the quality of  
life of citizens by facilitating  
transplantation and blood  
transfusion in the European Union*



*At the Organ Donation Day in Zagreb (Croatia) 2010, medical students formed a street performance and used bodies to shape a formation and simulation of a beating heart in the main city square of Bana Jelačića.*

*(EDD project, see later in this publication)*

Further information on the projects can be found:

— on the Health Programme Projects database at:  
<http://ec.europa.eu/eahc/projects/database.html>

— on the DG Health and Consumers Health Portal at:  
[http://ec.europa.eu/health-eu/index\\_en.htm](http://ec.europa.eu/health-eu/index_en.htm)

— on the DG Health and Consumers website at:  
<http://ec.europa.eu/health/>

The Executive Agency for Health and Consumers (EAHC) implements the EU Health Programme, the EU Consumer Programme and the EU Better Training for Safer Food Initiative. See more at:  
<http://ec.europa.eu/eahc/>

# Foreword

In medicine, blood, tissue and cell — as well as organ — transplants are used to provide treatments to our citizens. Blood and blood components are essential in major surgery and to deal with traumas and bleeding. Transplants of organs are life-saving for many patients with serious chronic conditions, allowing them to return to normal daily activities. Tissue and cell transplants help restore body functions like eye-sight, skin barriers or immunity.

The European Commission's role here is to develop high standards of quality and safety of substances of human origin used in medicine, as foreseen in the Treaty on the Functioning of the European Union.

Our aim is to ensure safety throughout the European Union, so that when a citizen needs blood, some tissue or even an organ, he or she can rely on the safety of these substances. Donations need to be checked for safety, both for the donor and for the future recipient. The consequent steps leading to transfusion and transplantation need to respect minimal safety and quality requirements. All these professional activities are therefore subject to appropriate oversight activities, including authorisations, inspections, vigilance and traceability.

These medical practices are progressing continuously and therefore require the know-how and expertise of all actors in the field. The European Commission's services work closely together with professional actors as well as with the national authorities who oversee activities within their respective countries.

One way to bring together such EU-wide expertise for the benefit of patients is through projects and actions supported under the EU Health Programme. This publication presents an overview of the many projects that pursue the objective of offering access to safe and high-quality therapies. Many such projects foster the sharing of knowledge amongst experts and authorities, and thus bring European added value to national efforts in providing safe and secure transplantation and transfusion therapies throughout the European Union.

I am confident that these projects will encourage all European organisations involved to continue to work together towards the common goal of improving the quality of life of European citizens.

**Tonio BORG**

*European Commissioner for Health*



# Introduction

Since 2003, about 50 projects and other activities have been funded by the European Union in the area of transplantation and transfusion, in the framework of the EU health and research framework programmes and other European funding schemes.

These projects and activities include exchanges of best practice, standards for inspections, manuals and registers as well as training workshops. Most of them directly contributed to the implementation and transposition of the three major directives in the field of substances of human origin (SoHO), namely: (1) Directive 2002/98/EC on 'setting standards of quality and safety for the collection, testing, processing, storage and distribution of **human blood and blood components**'; (2) Directive 2004/23/EC on 'setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of **human tissues and cells**'; and (3) Directive 2010/45/EU on 'standards of quality and safety of **human organs intended for transplantation**'.

This brochure introduces each project with a short summary and provides descriptions of their major outputs. It aims to give as comprehensive an overview as possible and to provide references for later in-depth reading. It furthermore aims to illustrate how the outcomes of the projects presented shape the safety of patients, medical professionals and donors in Europe.

Projects were selected according to their contribution to the implementation of the abovementioned directives and were not restricted to a particular funding scheme.

The publication has three sections, according to the projects' contribution to the implementation of the directives: projects in the area of blood and blood components (red background); projects in the area of human tissues and cells for transplantation (blue background); and projects in the area of organ donation and transplantation (orange background).

Projects have been summarised by means of desk research. In addition, interviews were conducted with project coordinators and participants. The main outputs are represented in graphical form and an information box has been provided for each project, giving references for further reading. This approach is intended to bring an 'outside' perspective on the projects and activities and to let the brochure serve as an overview for reference purposes.

*This brochure was produced by the Executive Agency for Health and Consumers (EAHC) in close collaboration with the Directorate-General for Health and Consumers of the European Commission. The agency, set up by the European Commission in 2005, has the mission, among others, of supporting the implementation of the EU health programmes, of disseminating knowledge and best practice generated by the actions funded and of fostering exchange and cooperation between European public health professionals.*

# Contents

Foreword.....	3
Introduction.....	4
List of acronyms.....	8
<b>Blood and Blood Components .....</b>	<b>11</b>
Overview of projects in this section.....	15
Development of a pan-European standard operating procedure (SOP) methodology reflecting European best practice within the area addressing the quality and safety of blood (EU-Q-Blood-SOP project).....	16
Development of pan-European standards and criteria for the inspection of blood establishments (EuBIS) .....	20
Creating a safe and sufficient donor population in Europe: comparing and recommending good donor management practice (DOMAINE) .....	24
EU Optimal Blood Use Project (EUOBU).....	28
Quality Systems in the Blood Transfusion Field including inventory Visits, Audits and Proficiency Testing Scheme (PTS) studies (CoE EDQM).....	32
Ad hoc cooperation between EC and the CoE/EDQM on specific matters related to human substances (blood) in order to further develop and strengthen EU policy actions in this field (TS066 CoE2011).....	36
Training sessions for inspectors in the field of blood and blood components (CATIE) .....	41
EU-wide overview of the market of blood, blood components and plasma derivatives with a particular focus on their availability for patients (EAHC/2011/Health/15).....	44
Improving the safety of blood and organ supply by creating the research infrastructure to monitor emerging pathogens and develop new screening tests (BOTIA).....	47
Genomics and Blood Substitutes for 21st Century Europe (EURO BLOOD SUBSTITUTES).....	50
Rapid SPR for parallel detection of pathogens in blood (RaSP) .....	54
Development of a Blood Screening Assay for Diagnosis of Prion Diseases in Humans (PRIONSCREEN).....	58

## Human tissues and cells for transplantation ..... 63

Overview table of projects in this section.....	67
European registry for organs, tissues and cells (EUROCET project).....	68
Joint Accreditation Committee ISCT Europe & EBMT (JACIE).....	72
European Union standards and training for the inspection of tissues establishments (EUSTITE).....	76
Promoting optimisation, safety, experience sharing and quality implementation for donation organisation and networking in unrelated haematopoietic stem cell transplantation in Europe (POSEIDON).....	81
European Good Tissue Practices (Euro-GTPs).....	84
Vigilance and Surveillance of Substances of Human Origin (SoHO V&S).....	89
European Quality System for Tissue Banking Project (EQSTB).....	94
Building reference compendia for the application of a single European coding system for tissues and cells (Eurocet128, EAHC/ 2011/HEALTH/03).....	98
Evaluation of legislation and related guidelines on the procurement, storage and transfer of human tissues and cells in the European Union — an evidence-based impact analysis (Tiss.EU).....	102
Reprogramming the immune system for the establishment of tolerance (RISET).....	107
Strengthen and develop scientific and technological excellence in research and therapy of leukaemia (CML, AML, ALL, CLL, MDS, CMPD) by integration of the leading national leukaemia networks and their interdisciplinary partner groups in Europe (European LeukemiaNet).....	112
Transplantation Research Integration across Europe (TRIE).....	117
Comparative analysis of medically assisted reproduction in the EU: regulation and technologies (SANCO/2008/C6/051).....	121
Analysis and comparison of testing methods and testing laboratories in the EU and third countries for the biological markers specified in the blood and tissues and cells Directives (SANCO/2008/C6/012).....	125

## Organ donation and transplantation ..... 131

Overview of projects in this section.....	135
Improving the knowledge and practice of Organ Donation (DOPKI).....	136
European Group for Coordination of National Research Programmes on Organ Donation and Transplantation (ALLIANCE-O).....	141
European Training Programme on Organ Donation (ETPOD).....	146
European Living Donation and Public Health (EULID).....	151
European Framework for the Evaluation of Organ Transplants (EFRETOS).....	156
European Living Donor Psychological Follow-up (ELIPSY).....	162
Developing Guidelines for the Organisation of a Public Organ Donation Day (EDD)....	166
European Quality System Indicators and methodology on Organ Donation (ODEQUS)....	173
Coordinating a European Initiative among National Organisations for Organ Transplantation (COORENOR).....	177
2 <sup>ND</sup> Conference on Organ Transplantation: Ethical, Legal and Psychosocial Aspects — Expanding the European Platform (ELPAT).....	184
Joint Action on Mutual Organ Donation and Transplantation Exchanges: Improving and developing deceased organ donation and transplantation programmes (MODE).....	188
Achieving Comprehensive Coordination in Organ Donation throughout the European Union (Joint Action ACCORD).....	193
European Training Course for Trainers in Transplant Donor Coordination in the European Union.....	199
Study on the set-up of organ donation and transplantation in the EU Member States, uptake and impact of the EU Action Plan on Organ Donation and Transplantation (2009–2015).....	204
Living Organ Donation in Europe (EULOD).....	208

# List of acronyms

<b>Accord</b>	joint action on achieving comprehensive coordination in organ donation throughout the European Union
<b>AFSSAPS</b>	Agence française de sécurité sanitaire des produits de santé (French Agency for the Safety of Health Products)
<b>ALLIANCE-O</b>	'European group for coordination of research programmes on organ donation and transplantation' project
<b>BIG V &amp; S</b>	Bologna initiative for global vigilance and surveillance
<b>BOTIA</b>	'Blood and organ transmissible infections agents' project
<b>B-PTS</b>	blood-proficiency testing scheme
<b>CATIE</b>	competent authority training on inspections in Europe
<b>CJD</b>	Creutzfeldt Jakob disease
<b>CoE</b>	Council of Europe
<b>Coorenor</b>	'Coordinating a European initiative among national organisations for organ transplantation' project
<b>DG SANCO</b>	Directorate-General for Health and Consumers
<b>Domaine</b>	'Donor management' project
<b>DOPKI</b>	'Improving the knowledge and practice of organ donation' project
<b>EAHC</b>	Executive Agency for Health and Consumers
<b>EATB</b>	European Association of Tissue Banks
<b>EBA</b>	European Blood Alliance
<b>EBMT</b>	European Group for Blood and Marrow Transplantation
<b>EC</b>	European Commission
<b>EDD</b>	'European donation day' project
<b>EDQM</b>	European Directorate for the Quality of Medicines and Healthcare
<b>Efretos</b>	'European framework for the evaluation of organ transplants' project
<b>Elipsy</b>	'European living donor psychological follow-up' project
<b>ELM</b>	European LeukemiaNet
<b>ELPAT</b>	'Ethical, legal and psychosocial aspects of organ transplantation' platform
<b>EMA</b>	European Medicines Agency
<b>EQSTB</b>	'European quality system for tissue banking' project
<b>ESHRE</b>	European Society of Human Reproduction and Embryology
<b>ESOT</b>	European Society for Organ Transplantation
<b>ETPOD</b>	'European training programme on organ donation' project
<b>EU</b>	European Union
<b>EuBIS</b>	'EU blood inspection' project
<b>EULID</b>	'European living donation and public health' project
<b>EULOD</b>	'Living organ donation in Europe' project
<b>EUMDS</b>	European Myelodysplastic Syndrome Registry

<b>EUOBU</b>	'European Union optimal blood use' project
<b>Eurocet</b>	'European Registry for Organs, Tissues and Cells' project
<b>Eurodonor</b>	'European Donors And Organs Registry' project
<b>EURO-GTP</b>	'European good tissue practices' project
<b>Eustite</b>	'European Union standards and training for the inspection of tissues establishments' project
<b>HSCT</b>	haematopoietic stem cells transplantation
<b>ICCBBA</b>	International Council for Commonality in Blood Banking Automation
<b>IFBDO</b>	International Federation of Blood Donor Organisations
<b>IMI JU</b>	innovative medicines initiative joint undertaking
<b>ISCT</b>	International Society of Cellular Therapy
<b>JACIE</b>	Joint Accreditation Committee ISCT Europe and EBMT
<b>MODE</b>	joint action for mutual organ donation and transplantation exchange
<b>NAT</b>	nucleic acid amplification technique
<b>NIVEL</b>	Netherlands Institute for Health Services Research
<b>Odecus</b>	'Organ donation European quality system' project
<b>OMCL</b>	official medicines control laboratories
<b>ONT</b>	Organización Nacional de Trasplantes (Spanish National Transplant Organisation)
<b>PBSC</b>	peripheral blood stem cells
<b>PICS</b>	pharmaceutical inspection cooperation scheme
<b>Poseidon</b>	'Promoting optimisation, safety, experience sharing and quality implementation for donation in unrelated HSCT' project
<b>Prionscreen</b>	'Development of a blood screening assay for diagnosis of prion diseases in humans' project
<b>PTS</b>	'Visit, audits and proficiency testing scheme' programme
<b>QA</b>	quality assurance
<b>QALY</b>	quality-adjusted life years
<b>QMS</b>	quality management system
<b>RaSP</b>	'Rapid surface plasmon resonance (SPR) detection of pathogens in blood' project
<b>RISET</b>	'Reprogramming the immune system for the establishment of tolerance' project
<b>SoHO</b>	substances of human origin
<b>SoHO V&amp;S</b>	vigilance and surveillance of substances of human origin
<b>SOP</b>	standard operating procedure
<b>SPR</b>	surface plasmon resonance
<b>TCO</b>	transplant coordination office
<b>TE</b>	tissue establishment
<b>Tiss.EU</b>	'Evaluation of legislation and related guidelines on the procurement, storage and transfer of human tissues and cells in the European Union' project
<b>TRIE</b>	'Transplantation research integration across Europe' project
<b>TPM</b>	Centre for Transfer of Knowledge, Technology and Innovation of Barcelona
<b>WHO</b>	World Health Organisation



# Blood and Blood Components



Blood and blood components are essential for healthcare in Europe. There is no major surgery without blood supply. Treatments of traumas, acute bleeding and several chronic diseases all rely on the availability of blood.

Blood cannot be manufactured; neither can it be stored over a long period. That is why hospitals need to rely on a continuous and safe supply of blood from donations — gifts from blood donors.

In Europe, healthcare for 500 million citizens depends on more than 20 million donations of blood given by almost 15 million donors. Thirty-seven per cent of the EU citizens have donated blood at least once in their lives. But when we look at the repeat donors the figures are much lower. Willingness to donate blood is also seen to be higher in the group of 40–54 year olds (46 %).

As laid down in Article 168 of the Treaty of the Functioning of the European Union, a common framework has been set up to ensure the safety and quality of blood, both for donors and for recipients. It is the role of the European Commission to ensure implementation of these requirements by the different actors in the field: from blood establishments collecting the donated blood to hospital blood banks bringing the blood (components) to the bedside of the patient in need of a transfusion.

Legally, the framework is laid down in Directive 2002/98/EC of the European Parliament and the Council of 27 January 2003 on setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components. Consequently, implementing legislation focuses on technical requirements for blood (components) (Commission Directive 2004/33/EC), on traceability requirements and notification of serious adverse reactions and events (alert situations) (Commission Directive 2005/61/EC) and on quality systems for blood establishments (Commission Directive 2005/62/EC).

The key requirements of the different actors in the field are to apply: (1) clear criteria to select donors, (2) laboratory testing of every blood donation, and (3) quality standards for processing donated blood. Additional requirements for effective oversight are laid down for the competent authority in each of the EU Member States. These include the need for authorisations and inspections as well as the setting up

of tracing systems allowing every blood bag to be followed and vigilance systems allowing prompt action in case of alerts.

There are however some concerns and issues that cannot just be dealt with through legislation. This is why the legal approach, focusing on safety and quality, is to be supported by well-targeted projects. During the last years, DG SANCO has been able to secure funding under the EU Health Programmes to work on several elements.

1. Quality and safety measures for blood and blood components are evolving continuously with technological developments. Legislation is therefore not always the adequate tool to reflect these continuous changes in detail. Some of these measures need rather to be laid down in practical hands-on guidance for the blood establishments acting in the field. The development of a pan-European standard operating procedure (SOP) methodology reflecting European best practice within the area has led to such practical guidance within the **EU-Blood-SOP project**. Consequently, this guidance needs to be brought at best to the different blood establishments in the field. At this point, the good collaboration between the European Commission and the Council of Europe's (CoE) European Directorate for the Quality of Medicines and Healthcare (EDQM) needs to be mentioned. The EDQM has a strong experience in offering such guidance to European countries (both within and outside the EU), amongst others through their 'Guide for the Preparation, Use and Quality Assurance of Blood Components', currently at its 16th version. The Commission supports this work, amongst others by funding an **ad hoc cooperation with CoE/EDQM** to ensure alignment and complementarity between their work and the EU legislation.
2. Testing of all blood donations is mandatory by EU legislation and is a key pillar of blood safety. It is, however, not sufficient to lay down in the legislation what tests are required; one should also be able to rely on the accuracy of these test results. The Commission has therefore supported several projects on the testing of blood, from the development of reliable routine tests (**Rapid SPR for parallel**

**detection of pathogens**) in blood to the execution of **proficiency tests by the Council of Europe** in order to ensure that test results are comparable and reliable in laboratories all over Europe.

3. Inspections are an important and basic tool in the hands of the national competent authorities in order to ensure safety and quality within the activities of the blood establishments in the EU. The Commission is supporting the development and dissemination of common pan-European inspection standards, in order to align these national inspections practices, and eventually to build mutual confidence between authorities in different EU Member States. The **EUBIS project** has assessed differences in national inspection practices and developed common standards. More recently, the **CATIE project** is organising training workshops to bring these common standards to different countries.
4. Blood is a scarce resource, it cannot be produced but is a gift from donors. It is therefore important that the limited supply of blood is managed efficiently. The Commission supported and intends to support several projects working on the supply and demand side of blood. The **EU Optimal Blood Use project (EUOBU)**

focused on health professional in order to improve the quality and rationalisation of clinical transfusion processes. The **DOMAINE project** focused on the assessment and management of donors in order to ensure a sufficient and reliable donor base.

5. The landscape of blood supply and demand is complex and involves many actors from donation to transfusion. Some of these actors are public, others are private. Member States have policies to ensure self-sufficiency of blood and blood components. In parallel the demand for donations is driven by the growing need and market of plasma derivatives. To map out all these different and complex factors, the Commission has ordered an **EU-wide overview of the market of blood, blood components and plasma derivatives**.

EU Health Programme funded projects aim to bring together expertise from a diverse set of professionals in the field and from authorities in the different Member States. They aim to develop and share knowledge to improve practices in the field of transfusion, and therefore to ensure a sufficient supply of safe and qualitative blood, blood components and blood products to patients in need all over Europe.

## Overview of projects in this section

Acronym	Title	Page
EU-Q-Blood-SOP	Development of a pan-European standard operating procedure (SOP) methodology reflecting European best practice within the area addressing the quality and safety of blood	16
EuBIS	Development of pan-European standards and criteria for the inspection of blood establishments	20
DOMAINE	Creating a safe and sufficient donor population in Europe: comparing and recommending good donor management practice	24
EUOBU	EU Optimal Blood Use Project	28
QS-TS programme	Quality systems in the blood transfusion field including inventory visits, audits and proficiency testing scheme (PTS) studies	32
	Ad hoc cooperation between EC and the CoE/EDQM on specific matters related to human substances (blood)	36
CATIE	Training sessions for inspectors in the field of blood and blood components	41
	EU-wide overview of the market for blood, blood components and plasma derivatives with a particular focus on their availability for patients	44
BOTIA	Improving the safety of blood and organ supply by creating the research infrastructure to monitor emerging pathogens and develop new screening tests	47
Euro Blood Substitutes	Genomics and Blood Substitutes for 21st Century Europe	50
RaSP	Rapid SPR for parallel detection of pathogens in blood	54
PRIONSCREEN	Development of a Blood Screening Assay for Diagnosis of Prion Diseases in Humans	58

## Development of a pan-European standard operating procedure (SOP) methodology reflecting European best practice within the area addressing the quality and safety of blood (EU-Q-Blood-SOP project)

*This project has received co-funding from the European Union in the framework of the **Public Health Programme 2003–2008** (Grant: 2004217).*

In the last decade, the introduction of advanced technologies for the collection, processing and testing of blood has required an equal advance in high quality and safety standards of blood and blood components.

Increasing importance has been laid on establishing effective quality management systems for blood establishments. Those systems are needed to optimise the control and monitoring of the complex and sophisticated processes followed by modern blood establishments. A key element of quality systems is to define a common quality policy using standard processes or operating procedures. Standard operating procedures (SOP) are detailed, written instructions that serve to achieve uniformity of the performance of a specific function and are an essential element of quality management systems.

With the adoption of Directive 2002/98/EC in 2002, the European Union established the legislative foundation for setting high levels of quality and safety for human blood and blood components throughout the blood transfusion chain in the European Union.

**47 % of blood establishments needed to improve SOPs due to the EU legislation**

To address the requirements of the Directive, and in particular the need to develop tools providing practical guidance on how to install and maintain quality systems in blood establishments in the EU Member States, the **EU-Q-Blood-SOP project** was launched in 2005, with a duration of 3 years.

Under the coordination of the Red Cross Blood Donor Service of Baden-Württemberg in Germany, the project involved 16 blood establishments from 16 European countries to cooperatively design and develop a methodology for the preparation of SOPs in blood establishments in Europe.

The project started by taking stock of existing SOP manuals and guidelines used in the 16 blood services involved in the project in order to

		<b>EUBIS</b>	
EU-SOP	Standard Operating Procedure (SOP)	Page 1 of 4	
Scope: Institution / Department (name the department or unit issuing the SOP)			
<p><b>SOP:</b>                  Document-Code (e.g. EU-SOP)                  Document-Version (e.g. Version 1.0)</p>			
<b>Title:</b> EUBIS SOP Master Document			
<b>Valid from:</b>		Effective date. Expiry date. A document control procedure must be established to guarantee a regular review of documents and to keep the history of documents (previous versions).	
<b>Replaces Version:</b>		Document-Code and Document-Version	
<b>Changes:</b>		<ul style="list-style-type: none"> <li>- Please describe the relevant changes that have been made in comparison to the previous version of the document</li> <li>- Reasons for changes</li> </ul>	
<b>Distributor:</b>		Original: Quality management office  Copy-identification number (Example): 1, 2, 3 etc.  the use of electronic copies is optional	
<b>Written by:</b>		<b>Reviewed and authorised by:</b>	
Date:		Date:	
Name of person(s)		Name of person(s)	
File name: EUBIS SOP Master Version 1.0.doc			

*EuBIS SOP template*

identify international and national SOP manuals and inspection practices already in place. This was done through a survey questionnaire designed to find out the current status of SOPs, their structure and regulations and/or related manuals. The survey was divided into four sections, each addressing questions related to basic validation, principal management requirements, areas of work (eg. donor recruitment, testing, management, logistics) and the way in which risks were identified and managed.

A survey report summarising the findings from the questionnaire identified a series of gaps and needs. For example, almost half of the participating blood establishments were of the view that their present SOP system required changes in light of the European blood legislation. Almost a third indicated demand for improved inspection systems by governmental authorities; a few indicated that their blood establishments were not inspected by government authorities. Overall, this preliminary and necessary work provided solid foundations upon which to move forward.

### Providing the tools

The aim of the EU-Q-Blood-SOP project was not to provide an operating procedure to be used in an institution; rather, it was to provide the tools through which each institution can build its standard operating procedures and translate it into a formal document. An SOP document is important in that it describes a regularly recurring operation that affects the quality of the process. Its purpose is to ensure that the operations are carried out correctly and in a consistent way.

The EU-Q-Blood-SOP project's final product is thus an SOP manual, jointly developed by the project's partners, that provides the methodology for creating an SOP comprising the basic quality elements. As the development of an SOP is a multi-step process that involves preparation, writing, conclusion and training, the manual is articulated into different chapters that address each step in both a descriptive and practical manner.

Numerous examples are provided with regard to master SOPs, special SOP formats for testing and equipments, and SOP examples covering critical quality activities. They could also be used to adapt existing procedures to comply with current EU requirements.

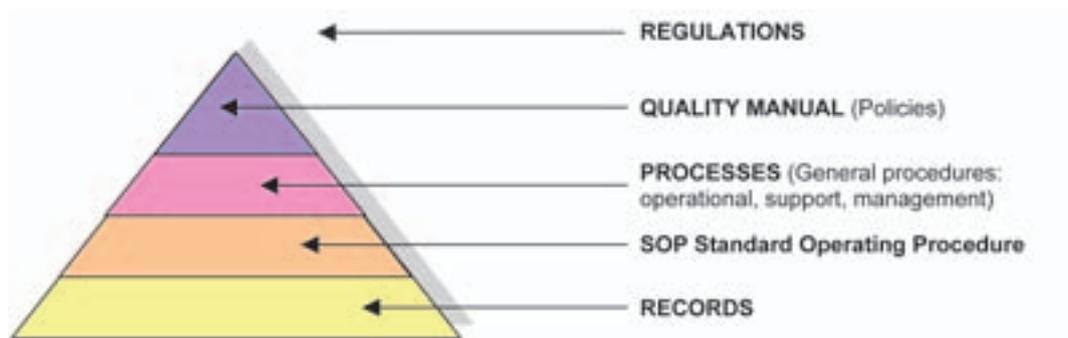
“ *The 2002/98/EU Directive is an important response to the need to protect public health and contributes to the high quality and safety of blood products and the preparedness to move blood in cases of pandemic crisis within the EU.* ”

<http://www.eu-q-blood-sop.de/index.php>



*European standard operating procedure (SOP) methodology reflecting European best practice within the area addressing the quality and safety of blood*

“ *‘Common standards for SOPs will assist the safety of blood and blood components.’* ”



This SOP methodology comprises precise quality requirements, requisites and quality terms linked to the EU Directives and is based on GLP/GMP standards that have to be specified (filled-in) in order to complete the documents. These quality requirements are presented in a modular fashion, in order to tailor the SOPs to meet local circumstances with respect to the differences in blood establishments and Member States.

In this context, the manual has been used by partners to consolidate or modify their existing SOPs system. During a twinning project between Germany and Malta, the Maltese blood transfusion service has used the manual in transforming its current document system into a system following best practice. In this respect, the manual or parts of it have been translated by its partners and collaborating

institutions into Czech, German, French, Romanian, Macedonian and Spanish in order to assist the dissemination on national and international levels.

Overall, the SOP manual delivers practical guidance on the basic structure for preparing SOPs. Its aim is to assist blood services to implement or improve their standard operating procedures to reflect European best practice.

The manual has been downloaded by more than 414 institutions, blood establishments, competent authorities and pharmaceutical industries from more than 62 countries in Europe and worldwide.



## EU-Q-Blood-SOP Project

Development of a pan-European standard operating procedure (SOP) methodology reflecting European best practice within the area addressing the quality and safety of blood.

### Further information:

EAHC Project Database:

<http://ec.europa.eu/eahc/projects/database.html?prjno=2004217>

Project website

<http://www.eu-q-blood-sop.de/>

SOP Manual

[http://www.eubis-europe.eu/blood\\_manual\\_details.php?ausgabe=sop#/10/](http://www.eubis-europe.eu/blood_manual_details.php?ausgabe=sop#/10/)

### Project team:

Project leader:

Red Cross Blood Donation Service Baden-Württemberg-Hessen, Institut für  
Transfusionsmedizin und Immunhämatologie

Sandhofstrasse 1

PO-BOX

60528 Frankfurt Am Main

GERMANY

Tel. +49 6967820

Fax +49 696782110

E-mail: EU-Q-Blood-SOP@blutspende.de

### Associated partners:

- The National Blood Authority (England and North Wales), United Kingdom
- Stichting Sanquin Bloedvoorziening (Sanquin Blood Supply Foundation), Netherlands
- L'Établissement français du sang, France
- Het Belgische Rode Kruis, Belgium
- The Blood Transfusion Service Board, Ireland
- Istituto Superiore di Sanita, Italy
- National Centre of Haematology and Transfusiology, Bulgaria
- Veobecná fakultní nemocnice v Praze (General Faculty Hospital Prague), Czech Republic
- Országos Vérellátó Szolgálat (Hungarian National Blood Transfusion Service), Hungary
- Instytut Hematologii i Transfuzjologii (Institute of Haematology and Blood Transfusion), Poland
- University of Medicine and Pharmacy 'Victor Babes', Romania
- Põhja-Eesti Verekeskus (North-Estonian Blood Centre), Estonia
- Ministry of Health of the Republic of Cyprus — Medical and Public Health Services, Cyprus
- Landspítalinn Háskólasjúkrahús (Icelandic University Hospital), Iceland
- Ċentru Nazzjonali tat-Trasfuzjoni tad-Demm (National Blood Transfusion Service), Malta

### EU contribution

This project has received co-funding from the European Union in the framework of the **Public Health Programme 2003–2008** (Grant: 2004217).

## Development of pan-European standards and criteria for the inspection of blood establishments (EuBIS)

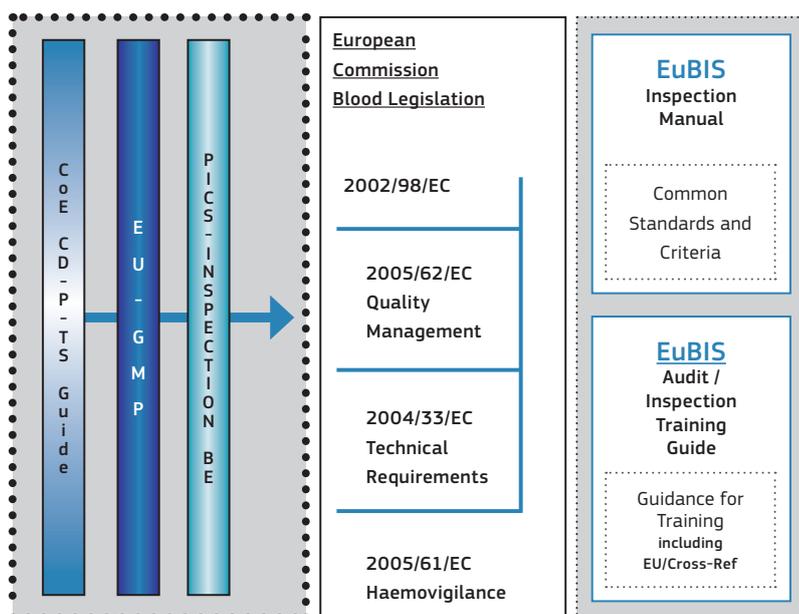
*This project has received co-funding from the European Union in the framework of the Public Health Programme 2003–2008 (Grant: 2006202).*

Ensuring that patients who receive blood transfusions in the European Union are given safe blood is a major objective of public health at national and European level. Significant progress has been made in recent years with the entry into force of EU legislation on blood, based on Directive 2002/98/EC and its technical annexes <sup>(1)</sup><sup>(2)</sup><sup>(3)</sup>. The Directives' main objectives are to ensure the provision of consistently safe blood components across Europe. The annexes set out the technical implementing measures for issues related to blood and blood components; traceability and the notification

of serious adverse reactions and events; and standards and specifications related to a quality system for blood establishments in the EU.

In many EU Member States, there are very rigorous regulations regarding blood donations and blood transfusions aimed at minimising the risk of a person being given blood that has been contaminated with a virus, such as Hepatitis C, or receiving blood from a blood group that is unsuitable for them. Inspection of blood establishments — namely of those structures or bodies involved in any aspect of the collection and testing of human blood or blood components and their processing, storage and distribution when intended for transfusion — is one key element of risk minimisation.

However, inspections of blood establishments are often conducted according to national criteria and standards which differ between Member States. Noting that divergent national regulations on the collection and treatment of blood were contributing to the reluctance, and at times refusal, to accept blood and plasma coming from different Member States and even different centres, the 2006 Work Plan of the Public Health Programme gave impetus to the need for equivalent recognition of inspections of blood establishments among Member States. This was to be achieved, amongst others, through the development and implementation of commonly accepted criteria and standards. Without them, the levels of risk from having a blood transfusion in the Member States could continue to differ.



*The EuBIS Project expert circle developed a manual for common European standards and criteria for the inspection of blood establishments for good practice (GP) following the EC blood legislation. (EuBIS — Common European Standards and Criteria for the Inspection of Blood Establishments)*

- <sup>(1)</sup> Commission Directive 2004/33/EC of 22 March 2004 implementing Directive 2002/98/EC of the European Parliament and of the Council as regards certain technical requirements for blood and blood components (OJ L 91, 30.3.2004, p. 25).
- <sup>(2)</sup> Commission Directive 2005/61/EC of 30 September 2005 implementing Directive 2002/98/EC of the European Parliament and of the Council as regards traceability requirements and notification of serious adverse reactions and events (OJ L 256, 1.10.2005, p. 32).
- <sup>(3)</sup> Commission Directive 2005/62/EC of 30 September 2005 implementing Directive 2002/98/EC of the European Parliament and of the Council as regards Community standards and specifications relating to a quality system for blood establishments (OJ L 256, 1.10.2005, p. 41).

### Reducing the risks of blood transfusion in Europe

The objective of the **EU-Blood-Inspection Project (EuBIS)**, was thus to set out a methodology for inspecting blood establishments. EuBIS has been coordinated by the German Red Cross Blood Donation Service with the participation of 27 collaborating partners from 21 Member States, cooperative working partnerships with five organisations and three projects, affiliations with 12 partners involved in conducting its

inspection survey, and is supported by the European Blood Alliance. As such, it is the first project to bring together regulators and manufacturers to jointly develop criteria and standards.

EuBIS activities got underway in September 2007. The first phase focused on the development and distribution of a questionnaire to the project's participants to collect information on current practices related to the inspection of blood establishments in the European Union. The results of a comparative analysis of the survey, in combination with Directive 2002/98/EC and its technical requirements, were used to establish the basic structure for the quality systems and pan-European blood inspection standards.

*“With the EU expansion, the implementation of common pan-European standards becomes even more important.”*

<http://www.eubis-europe.eu/>

Recognising that several inspection criteria and programmes in the healthcare area had already been established, from the outset the EuBIS project consulted these sources and conferred with the responsible authors. These included: the Joint Accreditation Committee of the International Society of Cellular Therapy (ISCT) and the European Group for Blood and Marrow Transplantation (EBMT) (jointly referred to as JACIE); the Pharmaceutical Inspection Convention and the Pharmaceutical Inspection Cooperation scheme (jointly referred to as PIC/S); and the European Medicines Agency (EMA). Moreover, EuBIS has collaborated and exchanged ideas with the EUSTITE (European Union Standards and Training for the Inspection of Tissues Establishments) project, co-financed under the 2005 Work Plan of the EU's Public Health Programme. EuBIS has indeed drawn extensively from EUSTITE's 'Guidelines for the Inspection of Tissue and Cell Procurement and Tissue Establishments'.

### **Comprehensive and collaborative efforts lead to the development of a good practice manual for the inspection of blood establishments in Europe**

In order to develop the basic structure of the manual, the project's participants were divided into four working groups, each with



*Common European Standards and Criteria for the Inspection of Blood Establishments* ([http://www.eubis-europe.eu/eubis\\_manual\\_details.php](http://www.eubis-europe.eu/eubis_manual_details.php))

responsibility for a specific subject area. These were: quality management system evaluation; donor recruitment and blood collection; processing and testing; and blood component issuing, storage and logistics.

The result of extensive collaborative efforts by the working groups has been a Manual that sets out common criteria and standards for the inspection of blood establishments; requirements for the implementation or expansion of quality management systems to be inspected; inspection checklists which closely follow Directive 2002/98/EC and its technical requirements, and evaluation criteria for inspections and a benchmark system for deviations and improvements.

Using commonalities between Member States and the requirements and definitions given by the EU blood legislation, the manual summarises good practice standards. The implementation of these standards can lead to improving



*Common European Standards and Criteria for the Inspection of Blood Establishments — Audit / Inspection — Training Guide*  
 ([http://www.eubis-europe.eu/eubis\\_manual\\_details.php](http://www.eubis-europe.eu/eubis_manual_details.php))

the safety of blood. This in turn can reduce the incidence of harm to patients that would otherwise arise from citizens travelling around the enlarged EU, and from the movement of blood components within the EU, either through the open-border policy or through crisis management measures.

### **An ongoing work: The EUBIS Academy Training Programme**

A major aim of the European Commission is to give practical assistance to competent authorities and blood establishments in implementing the Directive's requirements. Since the end of the project, the participants have founded the EUBIS Academy, which organises an annual training programme for inspectors of blood establishments based on the EUBIS manual and guide. This follow-up work is aimed at ensuring that the standards and criteria are commonly accepted. It offers the possibility to exchange knowledge and experience in setting up requirements in quality systems and inspection standards among participants from different EU Member States and internationally.

In addition, the EUBIS manual and guide have been integrated as a reference standard by the European Blood Alliance and are used by the quality management working party of the International Society of Blood Transfusion for its annual Academy Programme.

The EUBIS training programme included more than 70 trainees for the face-to-face training sessions and more than 800 participants in seminars. The manual and guide have been downloaded by 530 institutions (blood establishments, competent authorities and pharmaceutical industry) from 78 countries in Europe and worldwide.



### Further information:

EAHC Project Database:

<http://ec.europa.eu/eahc/projects/database.html?prjno=2006202>

Project website

<http://www.eubis-europe.eu>

SOP Manual

[http://www.eubis-europe.eu/blood\\_manual\\_details.php?ausgabe=sop#/10/](http://www.eubis-europe.eu/blood_manual_details.php?ausgabe=sop#/10/)

### Project team:

Project leader:

Red Cross Blood Donation Service Baden-Württemberg-Hessen, Institut für Transfusionsmedizin und Immunhämatologie

Sandhofstrasse 1

PO-BOX

60528 Frankfurt Am Main

GERMANY

Tel. +49 6967820

Fax +49 696782110

E-mail: [EuBIS@blutspende.de](mailto:EuBIS@blutspende.de)

### Associated partners:

- Landspítalinn Haskólasjúkrahús, Icelandic University Hospital, Iceland
- Ministry of Health, Elderly and Community Care, Malta
- University of Medicine and Pharmacy 'Victor Babes', Romania
- National Centre of Haematology and Transfusiology, Bulgaria
- Medical and Public Health Services — Ministry of Health, Cyprus
- Department of Blood Banking, Faculty Hospital Ostrava, Czech Republic
- Etablissement Français Du Sang, France
- Regierungspräsidium Darmstadt, Germany
- Hungarian National Blood Transfusion Service (HNBTS)/Országos Vérellátó Szolgálat (OVSZ), Hungary
- Irish Blood Transfusion Service, Ireland
- Irish Medicines Board, Germany
- Istituto Superiore di Sanità, Italy
- NHS Blood and Transplant, United Kingdom
- POHJA-EESTI VEREKESKUS, Estonia
- Institute of Haematology and Blood Transfusion, Poland
- Belgische Rode Kruis, Belgium
- Stichting Sanquin Bloedvoorziening, Netherlands

### EU contribution

This project has received co-funding from the European Union in the framework of the **Public Health Programme 2003–2008** (Grant: 2006202).



establishment of a safe and sufficient blood supply.

From 2008 to 2011, the DOMAINE project, which brought together 18 blood establishments from 18 European countries, one patient-driven organisation (Thalassaemia International Federation) and one representative from the south-eastern Europe Health Network, worked on improving donor management practices throughout Europe. *'It was a great experience. All partners were very enthusiastic and cooperative and willing to share their knowledge and experience with each other,'* says Dr Wagenmans.

Through a three-phase approach, the project concentrated on various aspects of donor management, including donor recruitment strategies, donor retention strategies, deferral procedures and blood bank policy regarding patients requiring long-term transfusion.

In the first phase, a survey was conducted to analyse donor management practice in Europe. This survey was sent out to participants and blood establishments in Member States, which were not involved as partner in the project. The International Federation of Blood Donor Organisations (IFBDO) and the Thalassaemia International Federation were also asked to comment on aspects of the blood donation process, and the relation between blood establishments and the blood recipients. By analysing the existing blood donor management practice across the EU, the DOMAINE project identified good practices, guidelines and performance indicators for donor management that were in place. The second phase focused on bringing this knowledge together into a manual on good donor management. The final phase aimed to train blood establishment professionals on the content of this manual.

### The Manual facilitates the implementation of good practice across Europe

The Donor Management Manual focuses on practical issues in donor management. It is aimed at donor managers and policymakers in the realm of blood donor management. The manual provides information on practical issues in donor management including: architecture and infrastructure; donor base; donor recruitment; donor retention; collection; multiple-transfused patients; special situations; human resources management; information technology; and ethical considerations.

Donor management for collecting blood products is a chain process, where each step depends on the success of the previous. The chain process consists of consecutive actions and steps, leading from donor recruitment to the required blood products.

Blood donors are recruited from the general population. People who are interested are called prospective donors. They form the pool of potential donors. Recruitment activities need to be targeted towards this group of prospective donors to raise blood donor awareness and to urge them to become blood donors. A certain number of prospective donors will actually decide to present themselves at a blood establishment to become blood donors. They will be registered in the donor data base as newly registered donors.

Registered donors who are eligible to donate will receive an invitation to make a donation. Donors can also be invited in a more general way through blood donation appeals through the media. In addition, there are people who visit the blood establishment spontaneously and will be registered on the spot.

Both personally and generally invited donors who do present themselves to donate are called attending donors. These donor candidates show up at the blood establishment to undergo medical screening (donor selection) determining donor eligibility. In some countries, the newly registered donor will only undergo a more or less specific selection procedure and laboratory tests. A donation procedure is not performed at this very first visit. When a donor is not eligible to donate, he or she receives either temporarily or permanently deferred status. Temporarily deferred donors will receive a new invitation to donate, while permanently deferred donors will be signed out of the donor data base. All donors who pass the donor selection successfully can make a donation. Most donation procedures are successful and will result in blood products. A small number of donations fail due to adverse events or unsuccessful procedures. Some of these complications can lead to a donor stopping his or her donor career. However, in general, successful donors will be invited again after a certain time interval.

A final step within the donor management process focuses on donor retention. Successful donor retention aims at minimising the population of permanently stopped donors. The pool of stopped donors is formed by no-show donors, permanently deferred.

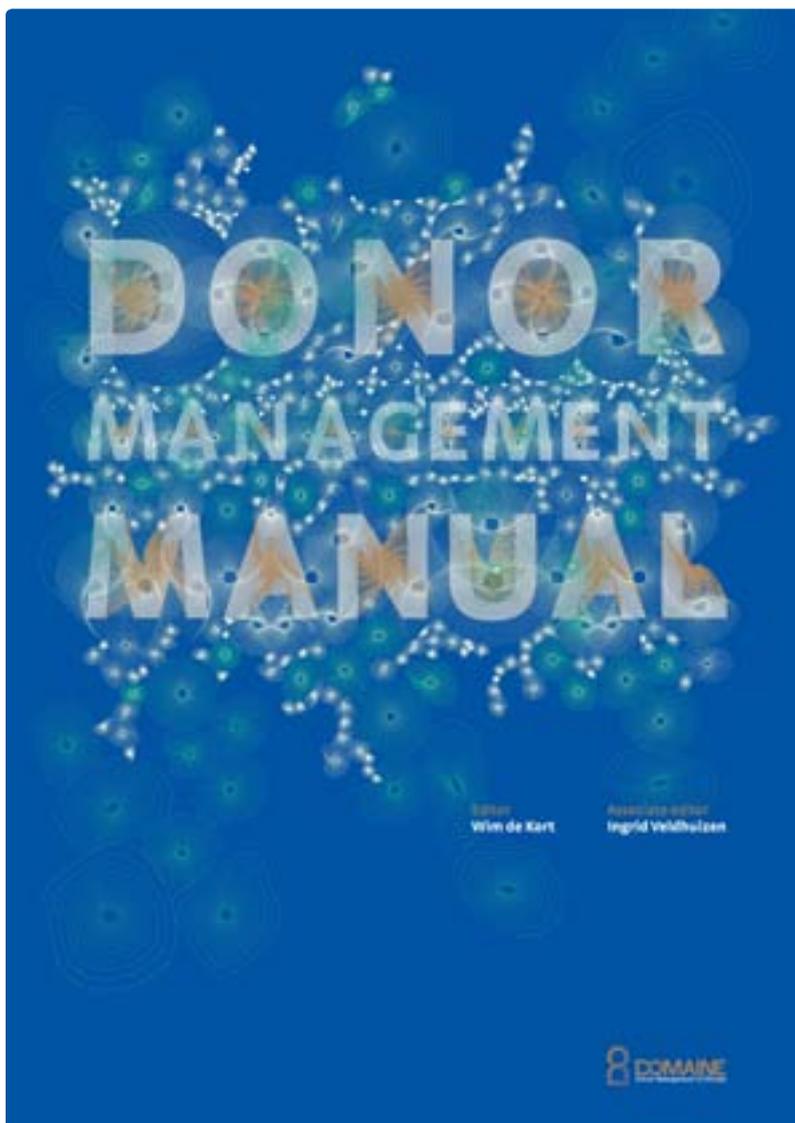
*The above is extracted from the Donor Management Manual. The manual further deals with collection; donor safety issues; multiple transfused patients; and special situations. (<http://www.domaine-europe.eu/Portals/0/Manual/Donor%20Mangement%20Manual%20final%20version%20part%201.pdf>)*

**“Doing things correctly facilitates all subsequent parts of the transfusion chain and make blood transfusion therapy safer and cheaper. Doing things incorrectly at this very first step affects the entire chain, often in an irreparable way.”**

<http://www.domaine-europe.eu>

“Almost 50 blood establishments from 34 European countries have contributed to the manual by sharing their information in the ‘voluntary, non-remunerated’ way, characteristic of the world of blood donation. The manual, therefore, brings together knowledge and experience in blood donor management from all over Europe.”

<http://www.domaine-europe.eu>



The DOMAINE Donor Management Manual focuses on practical issues in donor management. It is aimed at donor managers and policymakers in the realm of blood donor management.

The Manual serves as a toolkit to facilitate the implementation of good practice across Europe. It includes tools and examples of incentives to motivate future and current donors to become regular donors.

The Donor Management Manual is now available in five languages: English, Spanish, Portuguese, Dutch and French. The original, English version is both available as a book and in PDF form<sup>(5)</sup>. The Spanish, Portuguese and French versions are only available in PDF form.

### The Donor Management Training Programme continues beyond the project

A Training Programme for using the Donor Management Manual was also developed and established to provide practical tools on how each blood establishment can best use the Manual to achieve optimal practice within its local context. The training programme is aimed at managers and policymakers involved in any of the donor-related fields of activity, such as donor services, personnel management, marketing or facility management. It is based on the Donor Management Manual and addresses several topics that are organised in five modules: the donor management process, donor database management, donor marketing and communication, collection operations management and donor safety.

A ‘train the trainer’ approach was developed in the course of the project. Trainers equipped to distribute the Manual within their own country were trained. Each project partner delegated blood establishment professionals to participate in the Training Programme. These professionals were then able to implement the Manual in their own country and, as such, achieve sustainability of optimal donor management practice.

Since 2011, the training has been made available in conjunction with the training programmes of the EuBIS project and the Optimal Blood Use project under the coordination of the European Blood Association.

Overall, the project and its outputs have triggered a lot of interest at European and wider level. The manual itself is now also used outside Europe, in countries of south-east Asia, Africa and east Asia.

<sup>(5)</sup> <http://www.domaine-europe.eu/Manual/tabid/56/Default.aspx>



### Further information:

EAHC Project Database:

<http://ec.europa.eu/eahc/projects/database.html?prjno=2007202>

Project website

<http://www.domaine-europe.eu/>

Donor Management Manual

<http://www.domaine-europe.eu/Manual/tabid/56/Default.aspx>

### Project team:

Project leader:

Stichting Sanquin Boedvoorziening (SSB)

Plesmanlaan 125

1066 CX Amsterdam

NETHERLANDS

Tel. +31 243279034

Fax +31 243279471

E-mail: [w.dekort@sanquin.nl](mailto:w.dekort@sanquin.nl)

### Associated partners:

- Thalassaemia International Federation — TIF, Cyprus
- Ministry of Health, Elderly and Community care — MHEC, Malta
- Etablissement Francais du Sang — EFS, France
- Irish Blood Transfusion Service — IBTS, Ireland
- NHS Blood and Transplant — NHSBT, United Kingdom
- Blood Transfusion centre of Slovenia — BTCS, Slovenia
- DRK Blutspendedienst Baden-Württemberg Hessen GmbH — BSD-BH, Germany
- Medical & Public Health Services — CBE, Cyprus
- Het Belgische Rode Kruis — BRK, Belgium
- Országos Vérellátó Szolgálat / Hungarian National Blood Transfusion Service — OVSZ/ HNBTS, Hungary
- Austrian Red Cross — ARC, Austria
- Instituto Portugues do Sangue, IP — IPF / IP, Portugal
- Scottish National Transfusion Service — SNBTS, United Kingdom
- North Estonian Regional Hospital — Estonian Bloodbankers, Estonia

### EU contribution

This project has received co-funding from the European Union in the framework of the **Public Health Programme 2003–2008** (Grant: 2007202).

## EU Optimal Blood Use Project (EUOBU)

*This project has received co-funding from the European Union in the framework of the **Public Health Programme 2003–2008** (Grant: 2006209).*

A quality transfusion process is the ‘*transfusion of the right unit of blood to the right patient at the right time, and in the right condition and according to appropriate guidelines*’<sup>(6)</sup>.

The EU Optimal Blood Use project, launched in 2008 and co-funded by the European Commission Public Health Programme and the Scottish National Blood Transfusion Service for a duration of 3 years, aimed at promoting improvement in the quality of clinical transfusion processes. Through the collaborative

efforts of partners from 18 EU countries, the project has developed a resource, the Optimal Blood Use Manual, aimed at assisting professionals to improve the safety and effectiveness of the clinical transfusion process and to promote the optimal use of blood components across the EU.

### What is optimal blood use?

Optimal use of blood is the safe, clinically effective and efficient use of donated human blood. It is safe when there are no adverse reactions or infections. It is clinically effective when it benefits the patient. It is efficient when no unnecessary transfusions are performed and, when they are, these are done at the time the patient needs it.

### Why is optimal blood use important?

Blood is a human substance and is a precious and scarce resource, and many countries may at times encounter difficulties matching supply with demand. The supply of blood components in the EU depends substantially on the support of voluntary donors. Transfusion services promote blood donation as an essential contribution to the care of patients. Hospitals and blood collection services have thus an obligation to demonstrate to blood donors that each gift of human tissue is carefully, wisely and effectively used and that it can be fully accounted for. Patients themselves need assurance that blood is safe, available and used only when required.

The safety of hospital treatment and the effectiveness of care are major concerns in health-care systems. Some studies have shown that patients can suffer avoidable harm due to errors and accidents caused by quality failures in hospitals. These can occur in many aspects of the process of care, including in each of the main steps of the clinical transfusion process.

For example, errors in clinical decisions may lead to the wrong component or dose given; errors in ordering blood components may result in a patient receiving blood intended for another person; errors in pre-transfusion

“ *The manual is a resource for improving safety and effectiveness of the clinical transfusion process and promoting the optimal use of blood components across the EU.* ”

### Patients’ questions:

One way of introducing the concept of quality management in clinical transfusion is to consider some questions that any patient might ask if they believe that a transfusion may be given.

Here are some examples:

- Do I really need to have a blood transfusion?
- Will it help me?
- Could a transfusion do me harm?
- Will they give me the right blood?
- Will I feel unwell during the transfusion?
- If I start to feel bad during the transfusion will someone come to help me?
- If I need blood in an emergency will they get it to me in time?
- Will someone knowledgeable take the time to explain all this to me?
- Is the hospital staff properly trained to give me the transfusion?
- How do I know that the hospital does these things well?

*The above is extracted from the Manual of Optimal Blood Use — Support for safe, clinically effective and efficient use of blood in Europe ([http://www.optimalblooduse.eu/\\_assets/pdf/blood\\_use\\_manual.pdf](http://www.optimalblooduse.eu/_assets/pdf/blood_use_manual.pdf), p. 12).*

<sup>(6)</sup> [http://www.optimalblooduse.eu/\\_assets/pdf/blood\\_use\\_manual.pdf](http://www.optimalblooduse.eu/_assets/pdf/blood_use_manual.pdf)

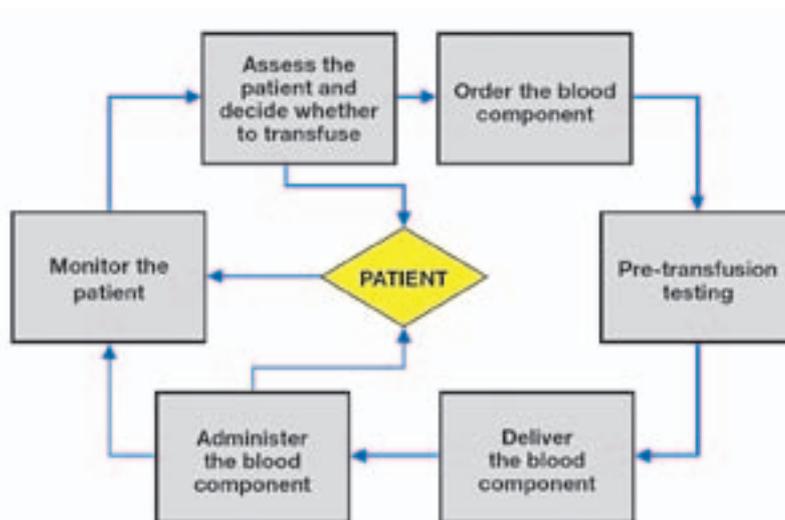
testing may include the selection of an inappropriate procedure or the non-checking of a patient sample and request for consistency and completeness; errors in delivering blood to the clinical area may produce delays in supplying blood; errors in administering (transfusing) blood may lead to the transfusion of an outdated pack or to a patient receiving an incorrect blood component; errors in monitoring the transfused patient may include the non-detection of adverse reactions or the incorrect management of such adverse reactions. The consequences of such errors range from the wasting of blood units to harm to the patient, risk of exsanguinations, serious complications and ultimately death.

For these reasons all hospitals should be in a position to ensure that their practice of blood transfusion is safe, clinically effective and efficient. Overall, a quality management system for transfusion is a key component of a hospital's wider quality system.

Developed through the sharing of information and best practices across the project's partners, the Optimal Blood Use Manual specifically addresses these issues. It is intended for hospital transfusion committees and for medical, nursing and laboratory staff who have responsibility for patient safety and the quality of care in relation to blood transfusion. It further serves other personnel who are concerned with quality improvement, risk management, accreditation, training and assessment. Patients concerned about the safety of transfusions can also find it useful.

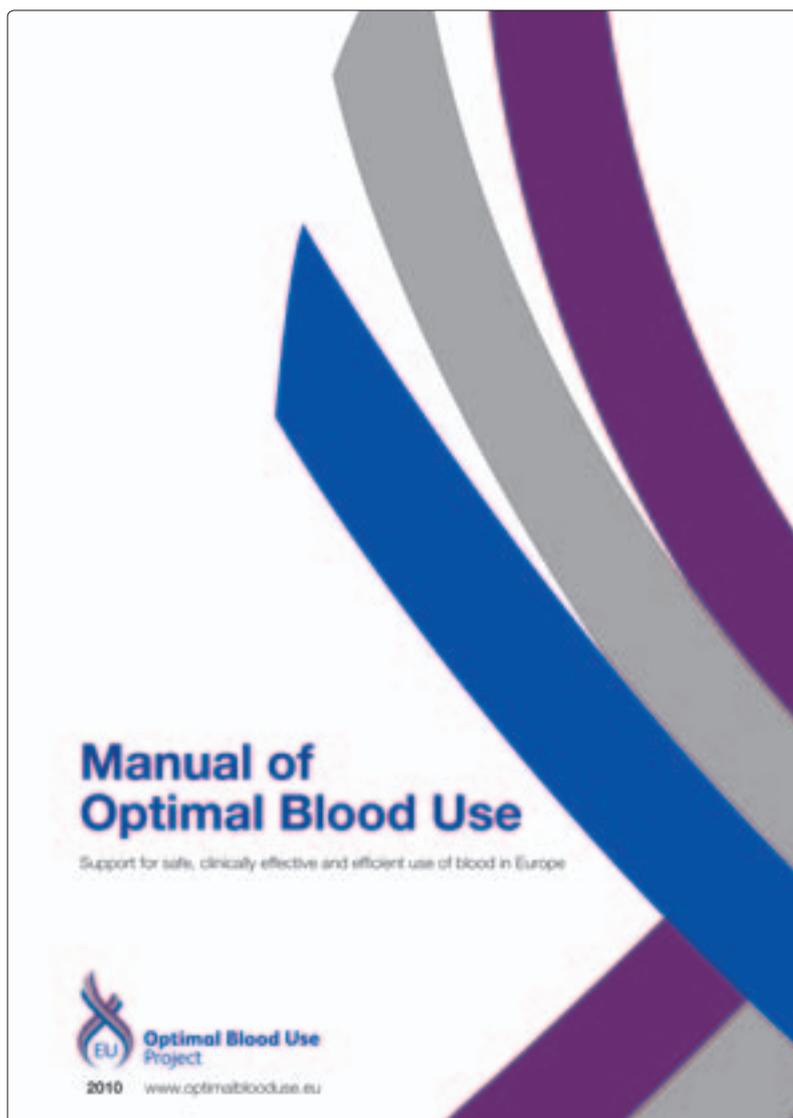
“*The Optimal Blood Use Manual provides guidance and resources to develop a quality system for the clinical transfusion process.*”

A quality system for the clinical transfusion process should provide assurance to patients, the community and clinicians that treatment is safe, effective and efficient and that the people who carry out each step of the process know what they are doing, how to do it and why they are doing it. It should provide evidence that tasks are carried out correctly and consistently using the right procedures. And it should lead to improvement in quality by providing evidence about performance and by encouraging everyone concerned to learn from both mistakes and successes.



Common steps of the clinical transfusion process and its infrastructure in EU countries

Source: <http://www.optimalblooduse.eu/content/1-synopsis>, p. 4



Manual of Optimal Blood Use — Support for safe, clinically effective and efficient use of blood in Europe.

## Evidence

For many important aspects of transfusion practice, there is not a firm basis of empirical evidence that identifies the most effective process or treatment. The manual provides an illustration of evidence-based practice recommendations with extracts from the 2009 guidelines of the Bundesaerztekammer (German Medical Association). In addition, the web version of the manual provides links to the underpinning evidence where there is high quality information as judged by established grading systems. An extensive database of clinical trials and systematic reviews of evidence relating to transfusion can be found at [www.transfusionguidelines.org.uk](http://www.transfusionguidelines.org.uk).

*The above is extracted from the Manual of Optimal Blood Use — Support for safe, clinically effective and efficient use of blood in Europe (<http://www.optimalblooduse.eu/content/24-evidence>).*

EC Directive 2005/62/EC requires that personnel in blood establishments shall be trained and assessed to be competent in their tasks. To facilitate the introduction of a quality system, the manual therefore includes a specific chapter on 'How to implement a training programme to support transfusion practice'. This provides an introduction to some of the practical issues that are likely to be encountered when applying the Directive's training and assessments requirements to all staff that have a role in the clinical transfusion process. The English version of the Manual has been translated into seven languages and is available online at: <http://www.optimalblooduse.eu/>



### Further information:

EAHC Project Database:

<http://ec.europa.eu/eahc/projects/database.html?prjno=2006209>

Project website

<http://www.optimalblooduse.eu/>

Manual of Optimal Blood Use - Support for safe, clinically effective and efficient use of blood in Europe

[http://www.optimalblooduse.eu/\\_assets/pdf/blood\\_use\\_manual.pdf](http://www.optimalblooduse.eu/_assets/pdf/blood_use_manual.pdf)

### Project team:

*Project leader:*

Scottish National Blood Transfusion Service

Ellen's Glen Road Liberton, Scotland

Edinburgh

EH17 7QT

UNITED KINGDOM

Tel. +44 135365978

Fax +44 135365961

E-mail: [merredith.hart@snbts.csa.scot.nhs.uk](mailto:merredith.hart@snbts.csa.scot.nhs.uk)

### Associated partners:

- Austrian Red Cross, Austria
- Põhja-Eesti Verekeskus, Estonia
- Blood Transfusion Centre of Slovenia (Zavod RS ZA Transfuzijsko Medicino (ZTM)), Slovenia
- University of Medicine and Pharmacy 'Victor Babes', Romania
- Institute Of Haematology and Transfusion Medicine, Poland
- Agenzia Regionale della Sanità — Regione autonoma Friuli Venezia Giulia, Italy
- DRK Blutspendedienst baden Württemberg Hessen gGmbH, Germany
- NHS Blood and Transplants, United Kingdom

### EU contribution

This project has received co-funding from the European Union in the framework of the **Public Health Programme 2003–2008** (Grant: 2006209).

## Quality Systems in the Blood Transfusion Field including inventory Visits, Audits and Proficiency Testing Scheme (PTS) studies (CoE EDQM)

*This direct agreement between the EC and the Council of Europe has received co-funding from the European Union in the framework of the Health Programme 2008–2013 (Grant: 20085301). This cooperation has been continued in 2011 (Grant: 20115101).*

The Visits, Audits and Proficiency Testing Scheme (PTS) Programme ensures that safe blood components can be obtained in neighbouring European countries when needed.

The provision of safe and compatible whole blood and labile blood components — such as plasma and erythrocyte concentrates — for transfusion and their appropriate use involves a number of processes. Each step in the processes brings its risks for errors — from the selection of blood donors and the collection, processing and testing of donated blood to the testing of patient samples, storage and the issues of compatible blood and its administration to the patient.

established, performed in a quality-focused way and continuously monitored to improve outcomes. The implementation of a quality system in the laboratory serves to reduce risk associated to blood transfusion, i.e. to ensure that appropriate tests are performed on the correct samples, that accurate results are obtained and that correct blood product is provided to the right patient at the correct time. To monitor the proper implementation of QS, visits, audits and proficiency testing scheme (PTS) studies should be regularly carried out.

Proficiency testing scheme studies are used by accrediting bodies and regulatory agencies to assess laboratory competence. It is a form of external quality testing using inter-laboratory comparisons to determine the performance of individual laboratories for specific tests or measurements and to monitor laboratories' continuing performance.

The laboratory aspect of the transfusion process is carried out in different ways across the European Union. In some settings, a local hospital blood bank manages the blood component inventory and the clinical blood transfusion laboratory services. In others, the blood establishment provides compatible blood directly to hospitals.

To ensure that the results obtained by the testing laboratories of blood establishments in Europe would be comparable and that performance quality systems (QS) including quality assurance (QA)<sup>(7)</sup> are maintained, appropriate systems need to be in place across the EU. At the launching of the QS-TS Programme in 2008, there was neither a European programme for quality assurance (QA)/quality system (QS) evaluation nor a proficiency testing scheme programme for testing laboratories in the blood transfusion field. Existing national

*“The on-site visits and proficiency testing programmes in the field of blood transfusion support the EU in fulfilling its Treaty obligation to set standards of quality and safety of substances of human origin for medical use.”*

*Direct Agreement QS-TS-CoE 20085301, Annex I*

The blood transfusion laboratories play a key role in the blood 'transfusion chain'. The aim of a blood transfusion laboratory in testing blood samples from patients and donors is to provide safe blood for transfusion. Transfusion laboratory practice relates to all processes and procedures put in place to achieve this aim. Quality failures in testing or other laboratory procedures can have serious implications for the recipients of blood and blood products.

### Quality testing is essential to reduce blood transfusion's risks

An effective quality system (QS) provides a framework within which activities are

<sup>(7)</sup> Quality assurance includes the entire process of providing patient care, from the time the physician orders the test until treatment of the patient based on the results of the test.

or local initiatives generally focused on a limited subset of testing methods and allowed for evaluation of laboratories at a national or local level only. Several countries did not have any comparable programme at all.

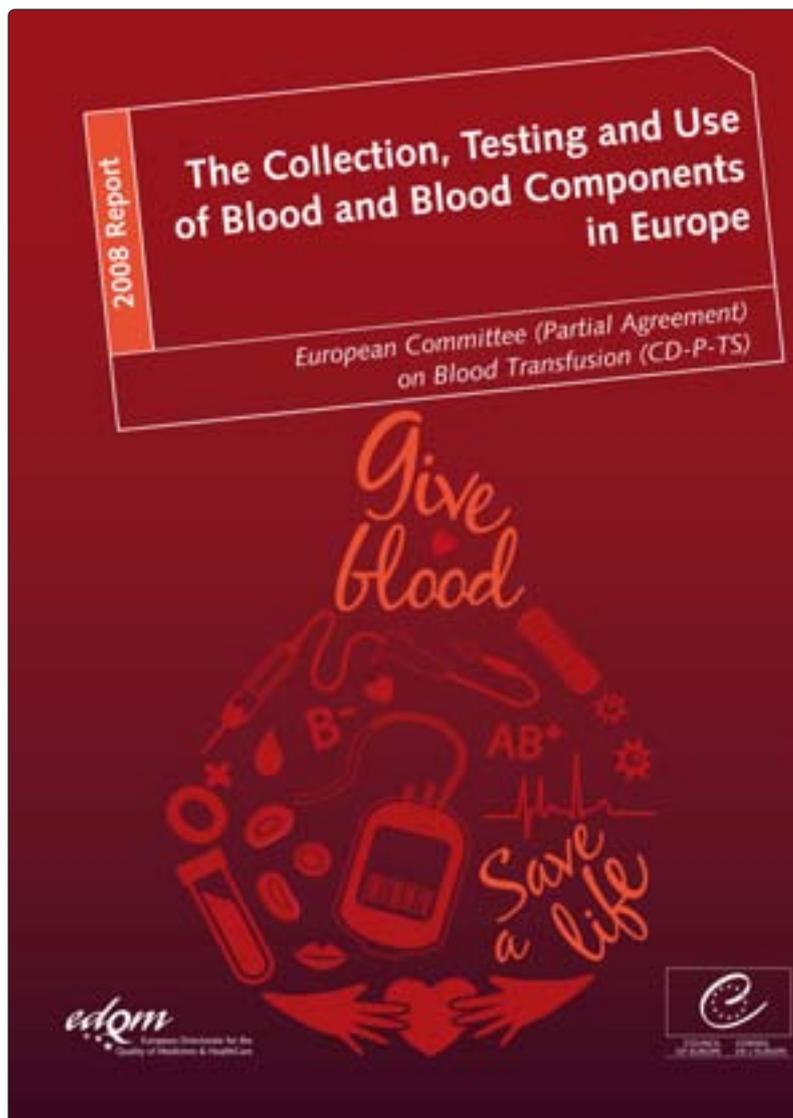
The QS-TS Programme was launched in 2008 to contribute to the establishment of an effective common system for quality assurance and performance measurement for whole blood and labile blood components screening and quality control in Europe. The programme was a joint initiative by the EC/EAHC and the Council of Europe. Managed by the European Directorate for the Quality of Medicines and HealthCare (EDQM) of the Council of Europe, its specific focus was on the proficiency of testing laboratories and in particular on undertaking proficiency testing scheme studies and an on-site visits programme.

The studies focused on the proficiency of testing laboratories responsible for the biological qualification of blood donations (screening for markers of transfusion-transmissible infec-

“ *The Blood-Proficiency Testing Scheme (B-PTS) Programme is ensuring safety by testing the reliability of laboratory results all over Europe.* ”

tions, e.g. HIV, HCV; characterisation of blood donations for immunohaematological markers, e.g. ABO erythrocyte antigen, rhesus, Kell antigen and other biochemical or hemostasis markers). The studies were accompanied by two on-site visits undertaken in the course of the project to assist testing laboratories in their preparation for audits and to help them implement state-of-the-art methods within appropriate QA environments.

During the course of the programme, priority was given to the tests which are required by Directive 2002/98/EC. Four PTS studies were carried out with 138 participating laboratories — between 24 and 43 for each study. The PTS studies were conducted on the detection of the Hepatitis C Virus by the nucleic acid amplification technique (NAT); the detection of the Hepatitis B surface antigen by serological assays; the detection of the Human Immunodeficiency virus by Nucleic Acid Amplification



Report on the Collection, Testing and Use of Blood and Blood Components in Europe.

Technique (NAT); and the detection of the Human Immunodeficiency Virus Antibody (HIV-Ab) by serological assays. The programme was open to all countries which are members of the EU and the Council of Europe, and 26<sup>(8)</sup> countries joined in.

### The programme is extended following demand in EU Member States

The programme was able to reveal failures in the completion of the abovementioned assays. Eleven laboratories were in fact classified by

<sup>(8)</sup> These were: Austria, Belgium, Bulgaria, Croatia, the Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Montenegro, Poland, Portugal, Serbia, Slovenia, Spain, Sweden, the Netherlands and the United Kingdom.

*“To maintain a high level of performance in the laboratory, it is essential to monitor the functioning of reagents, equipment, techniques and procedures. Good record keeping and documentation, use of standard operating procedures and laboratory worksheets, and implementation of safety guidelines further improve the quality of performance.”*

this programme as unsatisfactory, and have since been able to put in place corrective measures and preventive actions.

Marie-Laure Hecquet, the EDQM scientific officer in charge of this programme, notes *‘The blood establishments welcomed this initiative as the programme was tailor-made to blood establishments and was the first of this kind. Each study design is based on the methods and screening strategies used in blood establishments. Laboratories would like to see future developments in the programme, in particular to increase the number of PTS per year and enlarge the programme to other assays.’*

The programme was initially limited to a certain number of laboratories during the pilot phase. However, Marie-Laure Hecquet highlights that the contract has been renewed for 2 more years: *‘The programme is continuing as there is a great demand in all European countries and the programme is open to a greater number of laboratories. The co-funding from the EU and the*

*“The Council of Europe is, to be sure, the laboratory in which experiments in European cooperation are conducted.”*

*Robert Schuman, one of the founding fathers of the Council of Europe, 1951*

*Council of Europe is therefore really appreciated as it is expected to have a greater demand in the future.’*

The on-site visit programme was finalised at the end of 2012 and results have been reported. A survey to understand the European situation with regards to the implementation of the quality management system in European blood establishments was elaborated and sent in June 2012 to European blood establishments. More than 200 answers were received. The results show that there is a big demand for help in the implementation or further development of quality management systems (QMS) by establishments. The survey also shows that the norms and standards used for implementing a QMS are heterogeneous and varies between countries. *‘This would be the most challenging issue of the programme’* — notes Hecquet — *‘as support documents used to perform the visits, would have to take into account this specificity.’*

This programme helps laboratories themselves to improve their performance but also contributes to building mutual trust between European laboratories. **Results of PTS studies are a tool to demonstrate that safe blood**

**components can be obtained in neighbouring countries.**

This is of great importance in the context of issues raised on self-sufficiency and will establish a basis for reflection with regards to the exchange of blood

and blood components within Europe. Additionally, it will also provide feedback on the validation of the methods used in Europe in the field of blood transfusion.



### Further information:

EDQM website  
<http://www.edqm.eu/>

Blood transfusion guidance at EDQM  
<http://www.edqm.eu/en/blood-transfusion-mission-65.html>

The Collection, Testing and Use of Blood and Blood Components in Europe  
[http://www.edqm.eu/medias/fichiers/The\\_Collection\\_Testing\\_and\\_Use\\_of\\_Blood\\_and\\_Blood\\_3.pdf](http://www.edqm.eu/medias/fichiers/The_Collection_Testing_and_Use_of_Blood_and_Blood_3.pdf)

### Project team:

Project leader:

Department of Biological Standardisation, OMCL Network & HealthCare (DBO)  
European Directorate for the Quality of Medicines & HealthCare (EDQM),  
Council of Europe  
7, allée Kastner  
Cs 30026  
67081 Strasbourg  
FRANCE  
Tel. +33 388412152  
Fax +33 388412770

### EU contribution

This direct agreement between the EC and the Council of Europe has received co-funding from the European Union in the framework of the **Health Programme 2008–2013** (Grant: 20085301). This cooperation has been continued in 2011 (Grant: 20115101).

## Ad hoc cooperation between EC and the CoE/EDQM on specific matters related to human substances (blood) in order to further develop and strengthen EU policy actions in this field (TS066 CoE2011)

*This project has received co-funding from the European Union in the framework of the Health Programme 2008–2013 (Grant: 20105305).*

To provide all those working in the field of transfusion medicine — from blood services to hospital departments to regulators — with a compendium of measures designed to ensure the safety, quality and efficacy of blood components, the Council of Europe (CoE) developed a Guide as a technical annex to its Recommendation No R (95) 15<sup>(9)</sup> on the preparation, use and quality assurance of blood components in transfusion medicine.

The Guide<sup>(10)</sup> is now at its 16th edition and has grown to become the basis for a large number of national regulations, as well as for the blood directives of the European Commission. The latest edition of the Guide contains recommendations on blood collection, blood components, technical procedures, transfusion practices and quality systems for blood establishments.

It further contains recommendations for the establishment of a quality management system (QMS).

Directive 2002/98/EC and its implementing directives also set out European quality and safety requirements for blood and blood components. Implementing Directive 2005/62/EC specifically sets out standards and specifications relating to quality systems for blood establishments and requires that the Commission develop good practice guidelines for quality system standards and specifications.

This project was launched through the ad hoc cooperation between the EC/EAHC and the CoE/European Directorate for the Quality of Medicines and HealthCare (EDQM) on specific matters related to human substances (blood). Its aim is to develop such good practice guidelines.

*“The application of the common European standards for quality management systems (QMS) will ultimately improve the quality and safety of blood and blood components in the Member States and will lead to the implementation of comparable systems. Furthermore, it will avoid duplication of efforts between EU and CoE Member States and strengthen cooperation between different European stakeholders. Ultimately, it will reduce the risk of blood transfusions for patients and thus contribute to the improvement of public health in the Member States.”*

*Ad hoc cooperation with the CoE/EDQM, TS066 CoE2011, Technical Specification*

**The EC (DG SANCO) and the CoE work together to further develop and strengthen EU policy actions on quality management systems (QMS) in European blood establishments**

The objective of the project is to elaborate common European standards for quality management systems (QMS) to be implemented in blood establishments and hospital blood banks involved in the collection, testing, processing, storage and distribution of human blood and blood components. These standards aim to become the references on which blood establishments will develop, implement and maintain their QMS, and can even be used as a basis by authorities when inspecting blood establishments in the EU and wider Europe.

The CoE and DG Health and Consumers (SANCO) have respective regulations and guidelines applying in this domain. This work will allow the completion of these standards

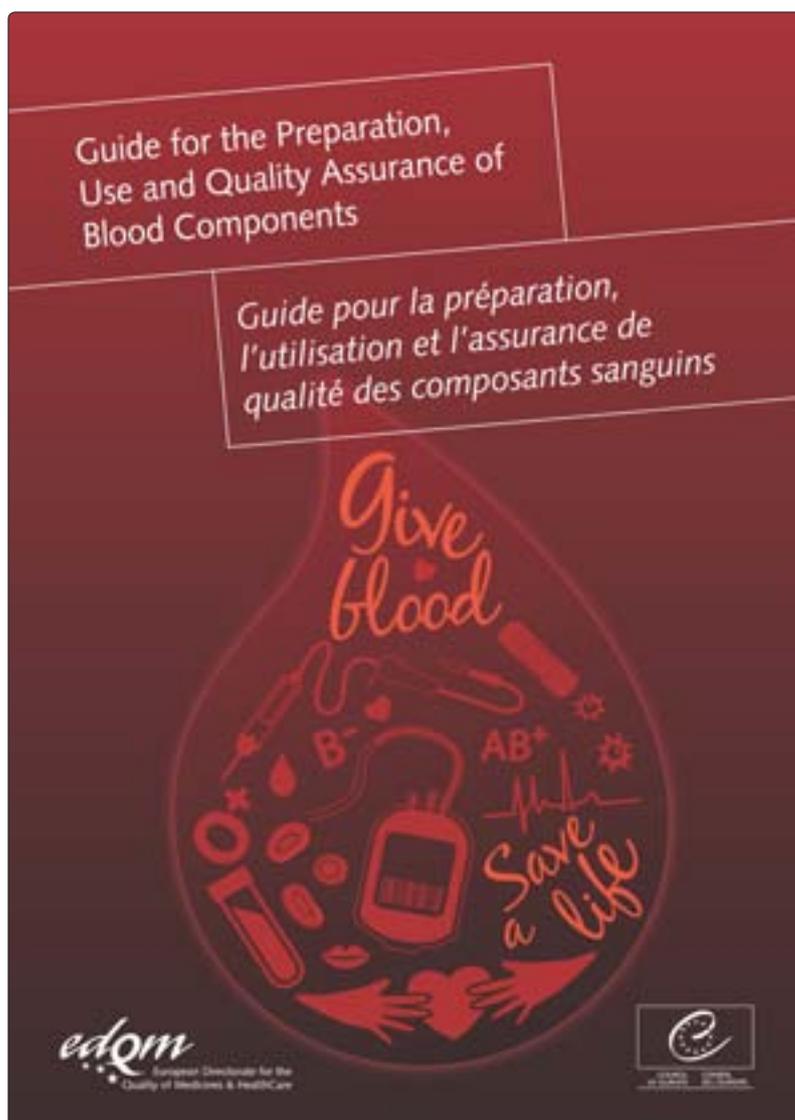
<sup>(9)</sup> [http://www.msc.es/profesionales/saludPublica/medicinaTransfusional/recomendaciones/docs/Rec95\\_15.pdf](http://www.msc.es/profesionales/saludPublica/medicinaTransfusional/recomendaciones/docs/Rec95_15.pdf)

<sup>(10)</sup> [http://www.centronazionalesangue.it/sites/default/files/guida\\_edqm\\_16\\_edizione.pdf](http://www.centronazionalesangue.it/sites/default/files/guida_edqm_16_edizione.pdf)

in order to establish a sound and updated common set of standards in QMS that are revised and approved by a group of recognised experts. At the same time, these standards can be fully aligned with the EU legislation in this field. While involving a larger number of states and countries, dissemination of those standards throughout and beyond Europe will support the harmonisation and diffusion of good practices. This may further help to prepare the way towards accreditation and will ensure that common standards will not only be applied by the EU Member States but also by the 47 Council of Europe Member States that are not part of the European Union. Such further step of harmonisation and standardisation of practices will be of benefit primarily to the safety of patients at a time when exchanges of substances of human origin and mobility of pathogens are continuously increasing.

This joint EU/Council of Europe project builds on the ongoing activities of the EDQM in the field of blood transfusion and other relevant documents used by the blood establishments, including Directive 2005/62/EC, the detailed principles and guidelines of good manufacturing practice (GMP), as referred to in Article 47 of Directive 2001/83/EC, and the outcome of related projects under the EU Health Programme (e.g. EU-BIS European Blood Inspection System<sup>(11)</sup>).

This collaborative effort led to the adoption of a commonly agreed document that was submitted for public consultation in the summer of 2012. Council of Europe Member State national health authorities and other interested parties in the blood field were invited to submit comments on the elaborated document. The finalised standards will be published in the 17th edition of the 'Guide to the preparation, use and quality assurance of blood components' in the course of 2013. This Guide is regularly updated to keep it in line with scientific progress. Therefore, these QMS standards will continue to evolve and improve with the rest of the Guide in the future.



*Guide for the Preparation, Use and Quality Assurance of Blood Components, 16th Edition.*

<sup>(11)</sup> <http://www.eubis-europe.eu/>

## **Guide for the Preparation, Use and Quality Assurance of Blood Components**

### **Why a European guide?**

In the field of blood transfusion, cooperation among Member States started back in the 1950s. From the outset, the activities were inspired by the following guiding principles: promotion of voluntary, non-remunerated blood donation, mutual assistance, optimal use of blood and blood products and protection of the donor and the recipient.

The Council of Europe has elaborated a guide on the preparation, use and quality assurance of blood components as a technical appendix to its Recommendation No. R (95) 15.

Work on Recommendation No. R (95) 15 started in 1986, when the Select Committee of Experts on Quality Assurance in Blood Transfusion Services published proposals on quality assurance in blood transfusion services. Based on these proposals, the Select Committee produced a more comprehensive guide on blood components in 1995. The immediate success and acceptance of this document was such that the Committee of Ministers adopted it as a technical appendix to the Recommendation No. R (95) 15.

This guide is a compendium of requirements designed to ensure the safety, quality and efficacy of blood components.

The Recommendation requires that the guide is updated to keep it in line with scientific progress. The European Committee on Blood Transfusion (CD-P-TS), the Steering Committee in charge of blood transfusion activities for the European Directorate for the Quality of Medicines & HealthCare (EDQM) of the Council of Europe, assisted by leading European experts, is responsible for producing regular updates.

This review includes a public consultation and comments are invited from national health authorities as well as all interested parties before a new edition is published.

### **Who is the guide designed for?**

The guide is a tool specifically designed for blood transfusion professionals working in transfusion services and establishments, hospitals and regulatory authorities.

### **What information does the guide contain?**

The guide contains standards and recommendations on blood collection, preparation and use of blood and its components, as well as technical procedures, transfusion practices and quality systems for blood establishments. It represents the basis for the establishment of national regulations and certain European directives.

### **Publication and purchase of the guide**

The guide is available in the two official languages of the Council of Europe (English and French). Other translations done either by the EDQM or under the responsibility of external parties and with the agreement of the EDQM are available (for example: Greek, Polish, Romanian, Russian and Turkish).

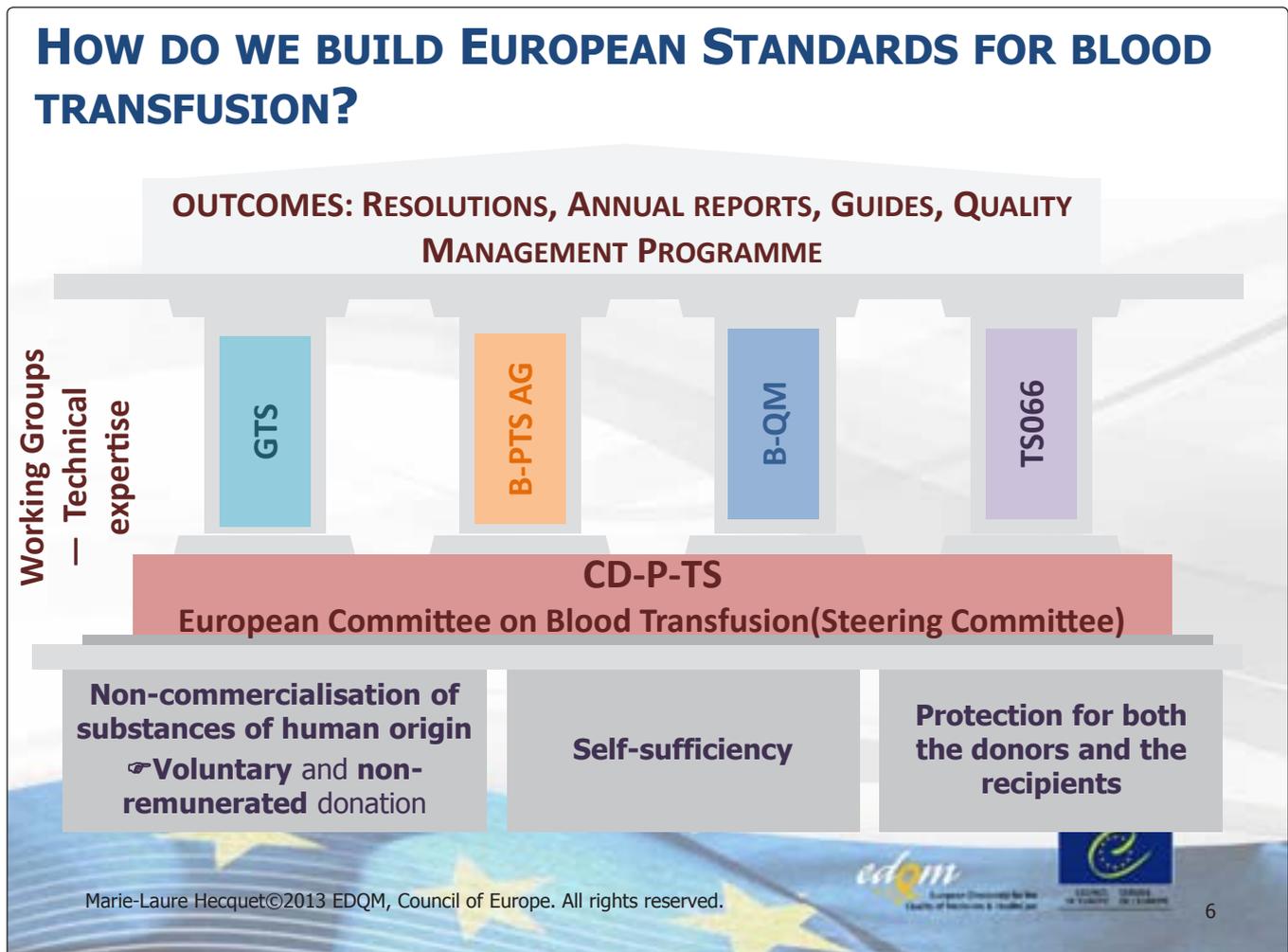
*The above is extracted from the General Information on the Blood Transfusion Guide (<http://www.edqm.eu/en/blood-organ-guides-1131.html>).*

## The EDQM

The European Directorate for the Quality of Medicines and HealthCare (EDQM)<sup>(12)</sup> of the Council of Europe is a European organisation involved in harmonisation and coordination of standardisation, regulation and quality control of medicines, blood transfusion, organ transplantation, pharmaceuticals and pharmaceutical care.

In 1997, the EDQM established a quality assurance (QA) programme open to all official medicines control laboratories (OMCLs), with the aim of ensuring a harmonised approach concerning

the implementation of quality management systems (QMS), based on the ISO/IEC 17025 standard 'General requirements for the competence of testing and calibration laboratories' and complemented by specific OMCL Guidelines. The QA programme, co-sponsored by the European Commission (DG Enterprise and Industry), includes inventory visits and audits. Since the beginning of the programme in 1997, 49 visits and 71 audits have been carried out at OMCL sites, by which the EDQM has gained considerable experience in the field of auditing and has offered a valuable tool to OMCLs to improve and harmonise their QMS.



<sup>(12)</sup> <http://www.edqm.eu/en/Homepage-628.html>



### Further Information:

EDQM website

<http://www.edqm.eu/>

Blood transfusion guidance at EDQM

<http://www.edqm.eu/en/blood-transfusion-mission-65.html>

The Collection, Testing and Use of Blood and Blood Components in Europe

[http://www.edqm.eu/medias/fichiers/The\\_Collection\\_Testing\\_and\\_Use\\_of\\_Blood\\_and\\_Blood\\_3.pdf](http://www.edqm.eu/medias/fichiers/The_Collection_Testing_and_Use_of_Blood_and_Blood_3.pdf)

### Project team:

Project leader:

Department of Biological Standardisation, OMCL Network & HealthCare (DBO)

European Directorate for the Quality of Medicines & HealthCare (EDQM),

Council of Europe

7, allée Kastner

Cs 30026

67081 Strasbourg

FRANCE

Tel. +33 388412152

Fax +33 388412770

### EU contribution

This project has received co-funding from the European Union in the framework of the **Health Programme 2008–2013** (Grant: 20105305).

## Training sessions for inspectors in the field of blood and blood components (CATIE)

*This service contract has been financed from the European Union in the framework of the Health Programme 2008–2013 (Call for Tender: EAHC/2011/HEALTH/13, Contract 20116101).*

The inspection of blood establishments is a key element in ensuring the quality and safety of blood and blood components in the EU. Yet, as highlighted by the earlier EuBIS project, differing national practices on inspections of blood establishments can contribute to reluctance, and at times refusal, to accept blood and plasma coming from different Member States and even different centres.

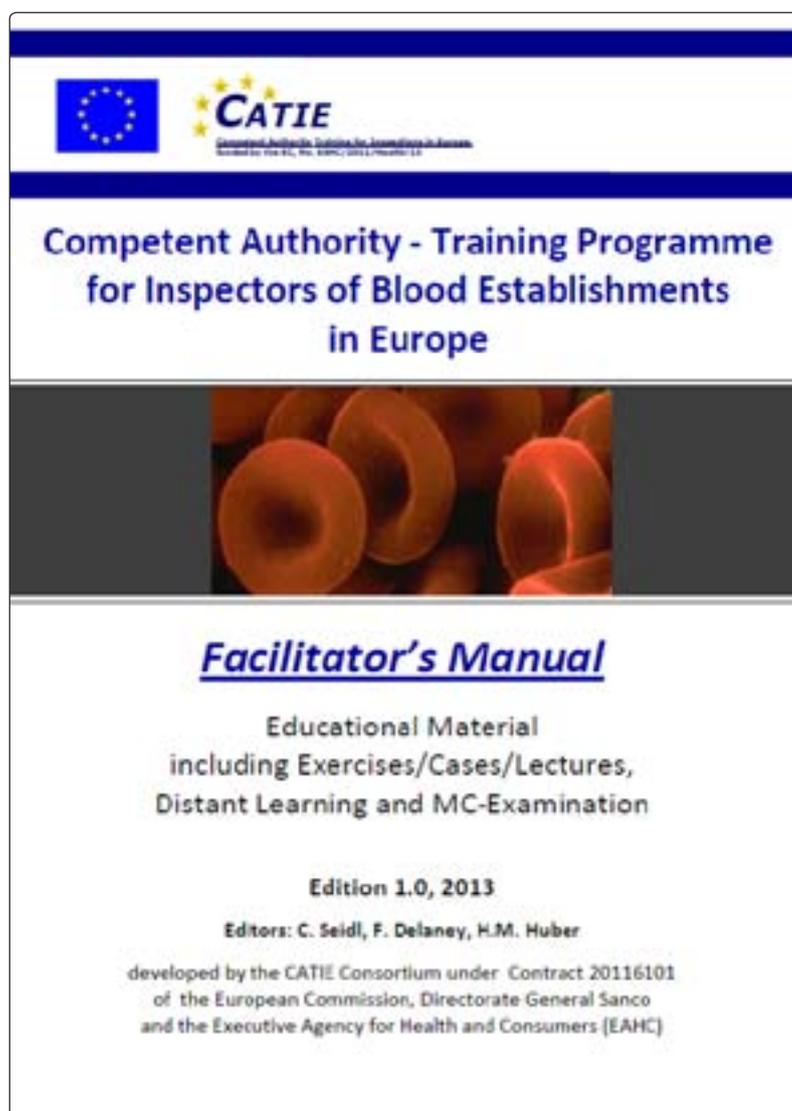
To align inspection practices and build mutual confidence between inspection systems, the European Commission's Directorate-General for Health and Consumer Affairs and the Executive Agency for Health and Consumers (EAHC) launched a call for tenders aimed at establishing a uniform set of knowledge and way of undertaking inspections across the EU and to further disseminate best practice and expertise.

The award was won by the CATIE consortium (Competent Authority Training on Inspections in Europe), composed of several competent authorities<sup>(13)</sup> in the field of safety and quality of blood products. Since January 2012, the consortium has worked to develop an inspectors' training programme on common standards and criteria for the inspection of blood establishments across the EU.

### Towards an EU common approach and methodology to prepare and conduct inspections in blood establishments

There is clear strategic value in the CATIE undertaking. Through the programme, in fact, inspectors will acquire an EU common approach and methodology to prepare and conduct inspections in blood establishments and will be updated on new methodologies and processes, including evaluation and managements of risks, quality assurance systems and vigilance and surveillance. At the EU level, this will contribute to establishing a common knowledge base

which will enhance trust and reciprocal understanding among competent inspections authorities across the whole EU. At national level, the enhancement of the inspectors' knowledge will contribute to reinforcing their two-fold responsibility — namely to ensure the quality and safety of blood and blood components and to ensure compliance with EU and national regulatory requirements.



<sup>(13)</sup> <http://www.catie-europe.eu/consortium-members-and-subcontractors.php>

Article 8 of the 2002/98/EC on **'Inspection and control measures'** states that 'Member States shall ensure that the competent authority organise inspections and appropriate control measures in blood establishments to ensure that the requirements of this Directive are complied with. Inspection and control measures shall be organised by the competent authority on a regular basis ... Such inspection and control measures shall be carried out by officials representing the competent authority who must be empowered to: (a) inspect blood establishments as well as facilities of any third parties on its own territory entrusted by the holder of the designation, authorisation, accreditation or licence ... ; (b) take samples for examination and analysis; (c) examine any documents relating to the object of the inspection, subject to the provisions in force in the Member States at the time of the entry into force of this Directive and which place restrictions on these powers with regard to the descriptions of the method of preparation.'

CATIE is thus working to develop training tools and materials that will be used by the competent authorities in the EU Member States for the purpose of regulatory inspections.

The training approach includes distance learning and training sessions. The distance learning modules aim to prepare trainees for the face-to-face training sessions (workshops). Trainees are offered preparatory material via the CATIE website to allow them to prepare for the workshops that follow this preliminary phase.

Each workshop is designed to last 4 days and consists of five modules: Module One comprises theoretical sessions on European regulations, processes, management of serious adverse events and reactions; Module Two is based on exercise sessions on risk identification, analysis, evaluation, reduction and review of events, classification of non-compliance and role-plays; Module Three focuses on on-site inspections; Module Four essentially consist of a final examination leading to a certification by DG SANCO/EAHC; and the last module includes an evaluation session.

The training material draws upon first-hand experience of inspectors involved in the consortium as well as on the manual and guide developed by the EuBIS project. For example, as part of the on-site inspection module, participants will be asked to use the inspection criteria and standards developed by the EuBIS project (manual and guide) including the corresponding documents to prepare the inspection.

The training package takes also into account other educational material developed by other projects funded by the EC, such as DOMAINE, EUOBU and EUSTITE.

Moreover, the composition of the consortium — which brings together competent authorities from different administrative structures and geographical background and thus represent different national regulatory inspection systems — helps to ensure that the educational material can be easily understood and adapted to the various national backgrounds of the trainees. The CATIE consortium is also affiliated to the European Blood Alliance (EBA) and the Pharmaceutical Inspection Convention/Scheme (PIC/S) Expert Circle on Blood and Tissue. While the EBA supports the CATIE consortium through its network of blood establishments, the PIC/S affiliation functions as a link to the regular workshops organised by PIC/S for inspectors. Further links are also established with the EDQM and the WHO.

The CATIE training was offered to competent authorities and governmental institutions of all EU Member States allowing for two to five inspectors per each of the 27 EU Member States to be trained. Four CATIE training courses were conducted — in Budapest (Hungary), Bilbao (Spain), Sliema (Malta) and Rome (Italy) — including a test following the distance learning and a final exam. Eighty participants from 31 countries (25 Member States) successfully completed the course. Their positive evaluations reflected their satisfaction with the course and the quality of the training.



### Further information:

Project website  
<http://www.catie-europe.eu/>

### Project team:

Project leader:

Red Cross Blood Donation Service Baden-Württemberg-Hessen  
Institut für Transfusionsmedizin und Immunhämatologie  
Sandhofstrasse 1  
PO-BOX  
60528 Frankfurt Am Main  
GERMANY  
Tel. +49 6967820  
Fax +49 696782110  
E-mail: [info@catie-europe.eu](mailto:info@catie-europe.eu)

### Associated partners:

- Paul-Ehrlich-Institut (PEI), Germany
- Centro Nazionale Sangue (CNS), Italy
- Autoridade para os Serviços de Sangue e da Transplantação (ASST), Portugal
- Ministerio de Sanidad, Política Social e Igualdad (MSPSI), Spain
- Agence Française de Sécurité Sanitaire des Produits de Santé (AFSSAPS), France
- Javna agencija Republike Slovenije za zdravila in medicinske pripomočke (JAZMP), Slovenia
- in coordination with the German Red Cross, Blood Donor Service (GRCBDS), Germany.

### EU contribution

This service contract has been financed from the European Union in the framework of the **Health Programme 2008–2013** (Call for Tender: EAHG/2011/HEALTH/13, Contract 20116101).

## EU-wide overview of the market of blood, blood components and plasma derivatives with a particular focus on their availability for patients (EAHC/2011/Health/15)

*This service contract has been financed from the European Union in the framework of the Health Programme 2008–2013 (Call for Tender: EAHC/2011/HEALTH/15, Contract 20116181).*

One of the main concerns of national health competent authorities for blood and blood components, as well as for the European Commission and international institutions like the World Health Organisation, are to maintain an adequate blood supply for patients requiring transfusion and to warranty the safety of the products for transfusion together with the prevention of the transmission of infectious diseases. At national level, few EU Member states report regular shortages of whole blood; however, occasionally, shortages of blood, blood components or plasma derivatives can occur.

“ *Self-sufficiency in safe blood and blood products based on voluntary non-remunerated blood donation means that the national needs of patients for safe blood and blood products, as assessed within the framework of the national health system, are met in a timely manner, that patients have equitable access to transfusion services and blood components, and that these products are obtained from voluntary non-remunerated blood donations of national, and where needed, of regional origin, such as from neighbouring countries.* ”

*WHO Expert Consensus Statement on achieving self-sufficiency in safe blood and blood products, based on voluntary non-remunerated blood donation (VNRBD), WHO 2011<sup>(14)</sup>*

Most countries have national policies for self-sufficiency of blood and blood components, yet less than half seem in fact to have defined the very concept of self-sufficiency.

Article 20(1) of the 2002 EC Directive<sup>(15)</sup> states that Member States should take the necessary measures to encourage voluntary unpaid

blood donation. The aim of promoting voluntary unpaid donation for blood products is to assist Member States in obtaining the maximum level of self-sufficiency for these products.

In March 2011 a report<sup>(16)</sup> on voluntary and unpaid donations in the EU was published by the European Commission. This report shows that Member States overall comply with Article 20(1) of the Directive requiring all states to take the necessary measures to ensure voluntary and unpaid blood donations are the main sources for whole blood and blood components provision. Results of the report show that legislative provisions and guidelines on voluntary and unpaid blood donation are also well established across the EU. Additionally, according to the report, 27 out of the 29 reporting countries promote policies to raise awareness for voluntary unpaid donations.

### There are public and private actors involved within the blood market

There are public and private actors involved within the blood and plasma market. There is a need to map the facilities and settings in the EU countries that collect, process (like fractionation<sup>(17)</sup> plants), store and distribute the final products, and all information regarding logistics.

A related aspect that needs further insight is the role and impact of the growing market of plasma derivatives on supply and quality aspects. Following the progress made by immunology science indicating the potential therapeutic applications of plasma fractions, over the last years the plasma industry has developed a wide range of products for the treatment of specific groups of patients. As

<sup>(14)</sup> [http://www.who.int/bloodsafety/Expert\\_Consensus\\_Statement\\_Self-Sufficiency.pdf](http://www.who.int/bloodsafety/Expert_Consensus_Statement_Self-Sufficiency.pdf)

<sup>(15)</sup> [http://ec.europa.eu/health/files/eudralex/vol-1/dir\\_2002\\_98/dir\\_2002\\_98\\_en.pdf](http://ec.europa.eu/health/files/eudralex/vol-1/dir_2002_98/dir_2002_98_en.pdf)

<sup>(16)</sup> [http://ec.europa.eu/health/blood\\_tissues\\_organ/docs/blood\\_reportdonation\\_en.pdf](http://ec.europa.eu/health/blood_tissues_organ/docs/blood_reportdonation_en.pdf)

<sup>(17)</sup> Fractionation refers to the general processes of separating the various components of blood plasma.

a consequence, the manufacturing of these medicinal products from plasma derivatives has significantly raised the demand for the plasma used by the pharmaceutical industry. This is why it is important to understand the impact of this increased need and how it affects the supply and donation of blood and plasma, particularly with regard to the fact that the demand for all these products is limited by the limited availability of donors.

Additionally, data on the economic aspects of this market including cost-effectiveness of the current practices for the collection, testing, storage and distribution will be of help for the preparation of guidance documents to help Member States to achieve self-sufficiency and also to verify the appropriateness of the current EU legislation.

In order to further develop the EU policy and legislation with regard to self-sufficiency and quality and safety of these products for transfusion, the European Commission is therefore funding a **study aimed at gathering and analysing information on the global and EU market of blood and blood components**, including plasma and plasma derivatives in the European Union.

The study is structured around some key areas. One focuses on the characteristics of the blood and blood component markets — such as market size, prices, actors, concerns and conflicts, supply and demand volumes and other elements in order to better understand these markets. A second area of focus is the mapping of the main actors involved in the blood and plasma derivatives markets, for each of the then 27 EU Member States and overall on the EU level, in order to better understand the roles and position of the public and private actors in this sector. A third area explores the impact of the growing market of plasma derivatives on supply and quality aspects of blood and blood products including plasma. This exploration is aimed at collecting information about the availability and supply shortages of those products in Europe in order to identify efficient utilisation practices in Europe and the movements of those products inside Europe — including bilateral agreements and the trade of these products between European countries and non-EU countries.

The study, launched in January 2012 for a duration of 14 months, is coordinated by Creativ-Ceutical.



### **Further information:**

Company's website  
<http://www.creativ-ceutical.com>

### **Project team:**

Project leader:

Creative Ceutical  
215, rue du Faubourg St-Honoré  
75008 Paris  
FRANCE  
Tel. +33 176704793  
Fax +33 153754924

And

33 Boulevard du Prince Henri  
1724 Luxembourg  
LUXEMBOURG  
Tel. +352 20880329

### **EU contribution**

This service contract has been financed from the European Union in the framework of the **Health Programme 2008–2013** (Call for Tender: EAHC/2011/HEALTH/15, Contract 20116181).

# Improving the safety of blood and organ supply by creating the research infrastructure to monitor emerging pathogens and develop new screening tests (BOTIA)

*This Specific Targeted Research Project has received co-funding from the European Union in the framework of the 6<sup>th</sup> Research Framework Programme (FP6-POLICIES Grant: 6487).*

In the western world, including western Europe and the US, blood and organ donors are routinely screened for a range of blood-borne viruses with highly sensitive tests. This has dramatically improved the safety of blood supply. However, we are far from being able to provide a 100 % guarantee on the safety of donated blood and organs. This is due to a range of different reasons.

One is the risk posed by new or mutated forms of infectious agents. At present, it takes many years to assess the dangers posed by these emerging pathogens and to develop measures to protect against them, and it is not even feasible to screen for all the pathogens we already know about. The bottleneck in this process is the lack of infrastructure required to conduct systematic and statistically sound studies on the relevance of newly discovered viruses and other agents in blood.

Appropriate and cost-effective screening procedures are not fully available. In this regard, the cost of genomic screening in developed countries is a major issue in blood transfusion because of its low cost-effectiveness. Additionally, many 'state-of-the-art' tests are not suitable for other parts of the world because they are complex, instrument dependent and expensive. As a consequence, the safety of the blood supply is less guaranteed in a number of countries.

## Immunodeficiency and latent viruses add further complications

There are also further issues related to immunodeficiency and to the difficulties in assessing the risks posed by latent viruses, such as herpes viruses. Many recipients of donated blood and organs have in fact some immune deficiency, placing them at greater danger from infection by these viruses. Immunodeficient blood/organ recipients have decreased natural resistance to viral infection and can be infected with considerably lower — often

even undetectable — amounts of virus than the immunocompetent counterpart. When the immune control breaks down, reactivation of both latent and persistent viruses can occur. This can have serious clinical complications.

## The BOTIA project set up an EU-wide sample repository to quickly assess blood-borne agents

The **BOTIA project (Blood and Organ Transmissible Infectious Agents)**, supported by a grant from the EU's Sixth Research Framework Programme (FP6) and involving seven European partners from Belgium, France, Germany, Italy, Poland, Spain and the United Kingdom, was developed to address these issues and to contribute to constitute a repository available for improving the safety of the blood supply and organ transplantation.

The project set up an infrastructure consisting of an EU-wide sample repository of paired donor and recipient samples to enable the fast assessment of emerging blood-borne agents and thus allow for appropriate measures to be taken without delay. This was done by establishing a European-wide collection of well-documented, linked samples from blood donors and their recipients, collected at pre- and post-transfusion. The collection of the samples was done over a 3-year period in order to obtain a large sample size and cover a large exposure period.

A computerised data management system, to enter information, track samples, manage and analyse data of samples and tests results, was then developed. This enables the selection of appropriate materials for studies when new infectious agents are detected.

At the Institut National de la Transfusion Sanguine, from where the project is coordinated, the BOTIA team highlights that *'The BOTIA project has demonstrated the efficiency of the collaboration of transfusion teams gathered*

**Scientific Support to Policies**

**Health**  
Taking the temperature of European healthcare

**BOTIA**  
Safer blood and organ donation in the face of emerging threats

*"To improve the safety of the donated blood and organ supply with new knowledge and new screening procedures."*

**The problem**

The safety of donated blood and organs is not fully guaranteed for several reasons. One is the risk from new or mutated forms of infectious agents. At present, it takes many years to assess the dangers posed by these 'emerging pathogens' and develop measures to protect against them. And it is not even feasible to screen for all the pathogens we already know about. There are also difficulties in assessing the risks posed by the fact that many recipients of donated blood and organs have some immune-deficiency, placing them at greater danger from infection.

**Overview:**

BOTIA will improve the safety of blood transfusion and organ transplantation.

The project will:

- Create an EU-wide repository of paired donor and recipient samples to allow fast assessment of emerging blood-borne pathogens and a quick response to the dangers they pose
- Identify emerging blood-borne pathogens using the latest genetic and biochemical techniques
- Locate limitations in current screening procedures for donated blood and organs, and develop improvements
- Produce specific recommendations that will help health authorities to tackle the problems

**Contribution to policy development:**

- Identification of deficiencies and failures of existing health policy frameworks in relation to the safety of donated blood and organs
- Provision of a research infrastructure that will decrease the response time of EU policy-makers when new threats arise or new techniques become available
- Development of a range of specific policy recommendations to allow health authorities to contribute to the safety of the blood and organ supply

Project description from the SINAPSE database (<https://europa.eu/sinapse/sinapse/>)

*“The clinical relevance of a blood-borne infectious agent is based on six criteria: transmissibility by transfusion/transplantation; pathogenicity; prevalence; persistence; availability of screening methods; and immune status of recipient. Currently, it takes many years before the clinical relevance of new/mutated pathogens has been assessed and appropriate measures taken.”*

<http://www.ints.fr/EuropIntBotia.aspx>

*around a common project. Such a success allows therefore envisaging further studies at the European scale on the topic of transfusion safety with regard to infections.'*

### **BOTIA turns into a 'permanent project'**

Such a European repository would, however, make no sense if its existence was limited in time. For some participating countries, the BOTIA project has turned into a kind of 'permanent project', allowing them to obtain biological materials on the infectious risk of transfusion at any given moment.

*'A strictly uniform European strategy for fighting blood-borne agents does not exist and is not to be wished, as each country has to take into account its own situation in relation to the prevalence, or even the existence, in its territory, of such transfusion-transmitted agents. In the case of the variant of the Creutzfeldt Jacob Disease (vCJD), for example, only two countries among the European Community — the United Kingdom and France — have been confronted with the risk. The situation was in no way the same in the other European countries. Consequently, a strategy based on identical safety rules for all European countries would make no sense,' notes the BOTIA team.*

Rather, the experience of a particular country in the field of transfusion safety may well be useful for other countries, in particular through the carrying out of common quality controls of biological tools for the screening of blood-borne agents, or in the constitution of a repository, which can be used for European studies aiming at the strengthening of transfusion safety. Indeed, this has been the purpose of this project.

## BOTIA

Safer blood and organ donation  
in the face of emerging threats

### Further information:

Project website

<http://www.ints.fr/EuropeIntBotia.aspx>

[http://ec.europa.eu/research/fp6/ssp/botia\\_en.htm](http://ec.europa.eu/research/fp6/ssp/botia_en.htm)

### Project team:

Project leader:

Institute National de la Transfusion Sanguine (INTS)

Prof. Philippe Rouger

6 rue Alexandre Cabanel

75739 Paris cedex 15

FRANCE

Tel. +33 143060483

E-mail: [prouger@ints.fr](mailto:prouger@ints.fr)

### Partners:

- Institute National de la Transfusion Sanguine (INTS), France
- University of Cambridge (UCAM), United Kingdom
- Ospedale A. Manzoni, Dipartimento di Medicina Trasfusionale e die Ematologia, Lecco (DTMH), Italy
- Scientific Institute of Public Health, Ministry of Public Health (IPH), Belgium
- Centre de Transfusio I Banc de Teixits (CTBT), Spain
- Academic Medical Centre (AMC), The Netherlands
- DRK Blutspendedienst Baden-Wuerttemberg-Hessen GmbH, Institut fuer Transfusionsmedizin (DRK BSD), Frankfurt/Main, Germany
- Reseumatique S.A., France
- Institute of Haematology and Transfusion Medicine (IHT), Poland

### EU contribution

This Specific Targeted Research Project has received co-funding from the European Union in the framework of the **6th Research Framework Programme** (FP6-POLICIES Grant: 6487).

## Genomics and Blood Substitutes for 21st Century Europe (EURO BLOOD SUBSTITUTES)

*This Specific Targeted Research Project has received co-funding from the European Union in the framework of the 6th Research Framework Programme (FP6-2002-LIFESCIHEALTH).*

Blood transfusion has its origins in the 1660s when Richard Lower, and later Jean-Baptiste Denis, began the first transfusions of blood, initially from animal to animal, and subsequently from animals to humans. In December 1818, James Blundell performed the first transfusion from one human patient to another, thereby laying the foundations for the dramatic refinements in transfusion practice and the establishment of blood banks which occurred in the 20th century.

Modern blood transfusion in industrialised countries is a universally practised and remarkably safe clinical procedure. Blood or concentrated ('packed') red cells are routinely transfused following extensive blood loss or as a treatment for chronic anaemia. In these situations, the aim of the transfusion is to not only increase blood volume, but also to increase the arterial oxygen content thereby enhancing the delivery of oxygen to the tissues.

“*What we are looking for is the powdered milk equivalent for blood.*”

*Professor Chris Cooper, Essex University — Euro Blood Substitutes project's partner*

potential to transmit diseases. Despite improved screening and processing, European citizens are becoming increasingly concerned about blood safety. Such concerns are making people more reluctant to donate blood or receive it through transfusions. In addition, blood is a scarce good with a limited supply, dependent on the willingness of individuals to donate.

Blood transfusion is not, however, a zero-risk intervention and there are several physiological and practical problems associated with this procedure. Blood is in fact a biologic material that has the

### Safe, effective and commercially viable blood substitutes can help to overcome blood transfusions' risks

Blood substitutes are oxygen-carrying fluids that aim to provide an alternative to the transfusion of blood. Put simply, they are fluids which, when injected into the blood, provide volume expansion and make a significant contribution to both systemic oxygen transport and tissue oxygenation. When coupled with the use of autologous blood (the patient's own blood or blood components), oxygen therapeutics will be a crucial part of future blood-conserving strategies to avoid patient exposure to donor blood and reduce the risk of contracting diseases transmissible via blood.

In 2004, a 12-member academic and industrial European team led by the University of Nottingham initiated the 3-year project **Genomics and Blood Substitutes for 21st Century Europe ('Euro Blood Substitutes')**. The aim of the project was to develop an integrated technological platform for generating blood substitutes for critical blood components, in particular oxygen carriers using microorganisms, such as bacteria and yeasts as living cell 'factories'. 'We're aiming to produce a replacement oxygen carrier, rather than a complete blood substitute because blood is a complex soup of materials that have many other roles besides carrying oxygen to the tissues,' explained Dr Lowe, the project coordinator.

Under the project, researchers worked to modify the genes of the oxygen-carrying part of the blood (haemoglobin) and used cell factories to mass produce artificial molecules that would be able to oxygenate the body's cells just as

efficiently, but without the possibility of contamination with disease.

In a 2005 interview preceding the presentation of the first project's results at the Society for Experimental Biology's annual meeting, Dr Lowe explained: *'We are using genomics to modify the haemoglobin as well as looking at ways to attach it to large molecules so that it stays in the body longer during transfusions. We are aiming to find the optimum molecules for oxygen-binding and transport as well as the best culture conditions for mass producing it for the future.'*

### The potentials for blood substitutes are as huge as the challenges posed by their production

The challenges faced by this new project were to both genetically engineer the microorganisms to synthesise haemoglobin (Hb) proteins, extract and purify them without adversely altering their biochemical characteristics, and to identify ways to scale-up the production of Hb to a commercial scale. Even a predicted annual use of a unit dose of ~50 g Hb in, say, 5 % of the European population was estimated to require the production of ~2 000 kg of protein — in itself a major commercial undertaking.

The project received major EU funding through the Sixth Research Framework Programme, since the potential for production of blood substitute components from microorganisms was considered huge. In principle, in fact, the use of blood substitutes could solve many of the problems associated with using blood for transfusion. Specific clinical targets have been identified for such blood substitutes, most especially their use to replace acute blood loss during surgery or following trauma. In people who refuse blood transfusions or those unable to receive transfusion for clinical reasons (e.g. patients with autoimmune haemolytic

Blood substitutes are needed and would be very helpful also on the battlefield. Which is why the American military first started researching the possibility of developing a synthetic blood substitute during the Vietnam War. It is very hard to have adequate amounts of blood in war zones, due to the rate at which blood expires. While the useful shelf life of donated blood when stored at 4 °C in a refrigerator is only ~42 days (even with the use of modern nutrient additives, such as mannitol, glucose and adenine), artificial blood has a longer shelf life (around 1 year) and can be stored at room temperature. It can also be universally given as it does not require different types for each blood type.

In countries with a high HIV prevalence, blood substitutes would be also particularly useful for blood transfusions. These countries usually cannot afford to test all blood that is donated. Therefore, people can become infected with HIV or other diseases through blood transfusions. If and when artificial blood becomes available in these regions, blood transfusions will become much safer and could even help reduce HIV transmission through blood transfusion.

<http://blogs.dickinson.edu/mindmeetsmatter/category/artificial-blood-artificial-oxygen-carriers/>

disease), an effective blood substitute could be life saving.

### Engagement with stakeholders

In addition to scientific research, the project also looked into the perceptions of benefit and risk associated with the transfusion of blood, blood products or, most especially, potential blood substitutes. As public attitudes play a crucial role in realising the potential of scientific and technological advances, the project conducted a survey (in the United Kingdom and the Netherlands) on what relevant stakeholder groups knew about transfusion; how safe people perceived blood and blood products to be; how the latter information would influence their own or others' perceptions of risk linked to transfusion; and to what extent approved blood substitutes would be preferred

### What blood substitutes are in development and how developed are they?

BLOOD PRODUCTS			
TYPE	EXAMPLES	STAGE OF DEVELOPMENT	NOTES
Donor Blood	<b>A, B, AB, O (+ / -)</b>	<b>Blood transfusions were developed in the 17th century.</b> Blood banks have been operating since the 1930's	Currently about 2.5 million units of blood are collected annually in the UK <sub>1</sub> . Approximately 5% of the population donates blood. Blood types must be matched; people can have one of four types of blood: A, B, AB, O each of which can be either positive or negative e.g. A+
Substitute made from Chemicals	<b>Perfluorocarbons</b> Oxygent	First-trialled in humans, 1978. Limited approval in the US	Perfluorocarbons are a liquid that can hold a lot of oxygen - enough to breathe when immersed in the liquid, but blood attracts oxygen whereas these chemicals only absorb it - so patients using perfluorocarbons as an oxygen carrier must breathe pure oxygen.
Substitute made from Cows' haemoglobin	<b>Hempure</b>	In clinical trials in the UK and USA; limited use in South Africa	Haemoglobin is the part of red blood cells, within blood, that attracts and holds oxygen. It is a protein with some iron in it. Some blood substitutes are based on this protein (because it is the crucial bit of blood for carrying oxygen). Bovine haemoglobin is relatively easily available and is quite robust, outside of red blood cells. Only the haemoglobin is used so other things in the cow blood are not transferred.
Substitute made from Human haemoglobin	<b>PolyHeme</b>	Clinical trials completed	Human haemoglobin is no more plentiful than donor blood so to make a blood substitute from human haemoglobin alternate sources of human haemoglobin have been used. One possibility is using GM technology make human haemoglobin. However haemoglobin outside of red blood cells is not very robust and can degrade so it needs to be further modified in some way to remain effective.
<b>LAST UPDATED APRIL 2006</b>			

<http://www.psychology.nottingham.ac.uk/staff/pff/euroblood/>

over a person's own or donor blood. Overall, the results<sup>(18)</sup> showed that donor blood was considered significantly more effective and more ethical than all the potential blood substitutes evaluated. Blood substitutes based on synthetic 'chemicals' (i.e. abiotic materials) were rated by respondents as similar to 'grown from bacteria' (recombinant Hb-based) substitutes in terms of effectiveness, but were viewed as more ethical. Substitutes based on 'cow blood' (bovine Hb) were perceived as the least ethical. All the blood substitutes were perceived as having similar effectiveness, albeit to a lower extent than for donor blood.

Information on what stakeholders perceive to be the benefits and risks of the receipt of blood and blood substitutes are important for future transfusion strategies and the design of new decision aids and physician training aids. This is particularly the case for blood substitutes as these become approved for routine clinical use.

<sup>(18)</sup> <http://www.psychology.nottingham.ac.uk/staff/pff/euroblood/results.htm>

### Further information:

Project website:

<http://www.psychology.nottingham.ac.uk/staff/pff/euroblood/index.htm>

CORDIS database:

[http://cordis.europa.eu/projects/rcn/75269\\_en.html](http://cordis.europa.eu/projects/rcn/75269_en.html)

Further:

<http://www.healthcompetence.eu/converis/publicweb/project/3337?show=Person>

### Project team:

The University of Nottingham

Dr Kenneth C. Lowe

University Park

Nottingham

NG7 2RD

UNITED KINGDOM

Tel. +44 1159513311

Fax +44 1159513251

### Other principal investigators:

- Andrea Bellelli (Universita degli Studi di Roma 'La Sapienza')
- Leif Bulow (Lunds Universitet)
- Michele Perrella (Universita degli Studi di Milano)
- Andrea Mozzarelli (Universita degli Studi di Parma)
- Chris Cooper (University of Essex)
- Patrick Menu (Universite Henri Poincare Nancy 1)
- Andras Eke (Semmelweis Egyetem)
- Jens Nielsen (Technical University of Denmark)
- Mats Andersson (Alligator Bioscience AB)
- Willi Glettig (LCC Engineering & Trading GmbH)
- Christopher Prowse (Common Services Agency)
- Agatha Brand (Sanquin Blood Supply Foundation)

### EU contribution

This Specific Targeted Research Project has received co-funding from the European Union in the framework of the **6th Research Framework Programme** (FP6-2002-LIFESCIHEALTH).

## Rapid SPR for parallel detection of pathogens in blood (RaSP)

*This Specific Targeted Research Project has received co-funding from the European Union in the framework of the 6<sup>th</sup> Research Framework Programme (FP6-2005-SSP-5-A, Grant: SP5A-CT-2006-044515).*

While blood transfusions, tissue transplantation or organ transplantation can be life-saving, they are not without risks. Blood establishments need to screen donors for risk factors and test donated blood to reduce the risk of transfusion-related infections, but they occasionally still occur. It usually takes 12 hours of laboratory work to know whether a blood sample is safe. This is already quite a long period of time in the case of blood donations, and it can be too long a time for organ transplantations.

The lab technologies used for screening diseases such as HIV and hepatitis therefore need to be improved — both in their capacity to detect pathogens and in their ability to deliver speedy results. In addition, there is a need to test donor blood in a cheap and fast way, especially in less developed countries where the rate of infected blood is high due to high prevalence of diseases.

The **Rapid SPR for parallel detection of pathogens in blood** (RaSP) project, that ran from 2007 to 2009 with EC co-funding through the FP6, took up these challenges.

Combining the interdisciplinary know-how of three research institutes, three university departments and three companies located in Europe, associated states and international

cooperation countries, RaSP has been able to develop a very fast, cheap and at the same time very sensitive method to simultaneously detect the pathogens HIV, Hepatitis C, Hepatitis B and syphilis. The method developed by the project has the additional potential to detect more than 100 blood pathogens simultaneously.

### RaSP develops a simple desktop method to detect multiple pathogens

*'Once the method will be implemented in a real product, the analysis will be done with a simple and small desktop system which is easy to use and which produces accurate results able to detect the presence of multiple blood pathogens,'* explains Dr Velten, the project coordinator. Within 10–20 minutes the doctor will know whether there are any pathogens, in the blood. Infected blood could then be immediately excluded from the blood banking procedure.

RaSP aimed to exploit a new type of surface plasmon resonance (SPR) transducing principle that allows a significant increase of sensitivity compared to the state-of-the-art SPR systems.

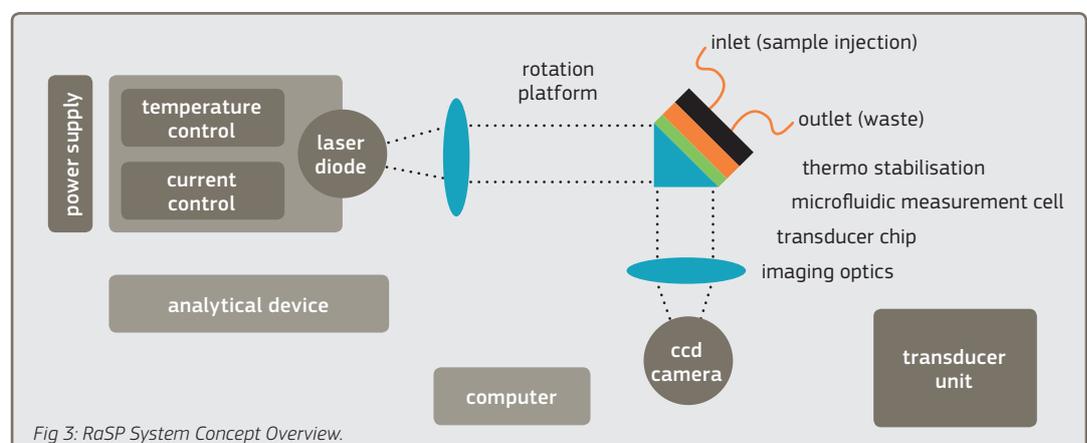


Fig 3: RaSP System Concept Overview.

### RaSP System Concept Overview<sup>(19)</sup>

<sup>(19)</sup> <http://www.rapid-spr.com/documents/Emerging%20Epidemics%20Research.pdf>

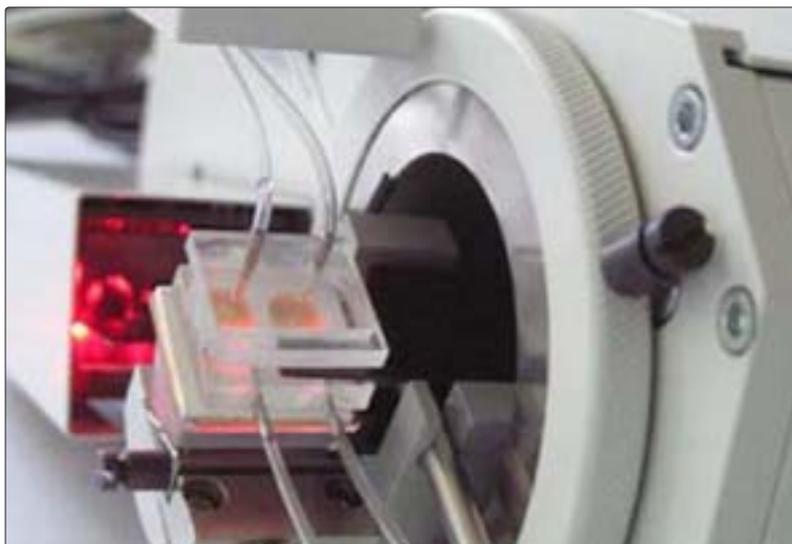
The immunosensitive diagnostic assay<sup>(20)</sup> is based on the very specific immune reaction between antigens and antibodies. More concretely, the project has developed a glass chip covered with antibodies; tiny surface oscillations are induced in the chip and if the relevant virus binds with an antibody, the oscillation changes. While the technique is not new, the chip that has been newly developed offers new advantages, in particular the fact that the new chip is more resistant to fluctuations in temperature. Additionally, the new chip consists of four analysis squares, which means that the blood can be examined for four different pathogens during each single test.

The chip is encapsulated, which makes the blood follow a defined course on the chip. Blood samples put onto the chip will not come into contact with the user nor with the non-disposable parts of the RaSP analytical instrument. Thus any contamination of the user and the RaSP instrument can be avoided.

### The prototype compares favourably with conventional methods

The capabilities of the first RaSP prototype system were evaluated in two countries by performing experiments with clinical samples that were compared with the results of conventionally used methods like ELISA. The measurements were performed by using transducer slides with immobilised antigens and antibodies against the four pathogens Hepatitis B and C, HIV, and *Treponema pallidum*<sup>(21)</sup>. 'A remarkable result of the performed experiments was the sensitivity to antibodies of Hepatitis B, because it was the first documented application of multiple SPR-technologies for the direct analysis of clinical samples. The comparison with ELISA showed a value of the correlation coefficient between these techniques of about 43 %,' notes Dr Velten.

Two different standard operating procedures (SOP) were developed for the work with real samples. The first method (SOP 1) is based on the signal observed after the replacement of a reference liquid by the serum that is to be analysed. Its main advantage is the short



A two-channel SPR for parallel or differential SPR measurements in liquids or in gases with wide angle range up to 17 degrees<sup>(22)</sup>

measurement time of about 10 minutes. SOP 2 is based on the measurements of changes of the SPR signal after the dissociation of the antigen-antibody complex in acidic conditions. In contrast to SOP 1, this procedure requires a longer measurement time of about 40 minutes but it is less influenced by non-specific effects and is not sensitive to variations of the refractive index of the clinical samples. Dr Velten however says that 'Although the first results were promising and confirmed the feasibility of the RaSP method there is still a long way to go from the first prototype to a real product.'

**“ This diagnostic method represents a revolution in the field of rapid diagnostics. It can be conducted in one step, on location where the blood is collected from donors, and it does not need any sophisticated laboratory preparation. Its applications in the medical sector will reduce the risk of dealing with contaminated biological materials and help to prevent persons from risks posed by contaminated blood. ”<sup>(23)</sup>**

<sup>(20)</sup> An assay is a quantitative or qualitative test of a substance to determine its components; frequently used to test for the presence or concentration of infectious agents or antibodies, etc.

<sup>(21)</sup> *Treponema pallidum* is a bacteria with subspecies that cause treponemal diseases such as syphilis, bejel, pinta and yaws.

<sup>(22)</sup> <http://www.rapid-spr.com/>

<sup>(23)</sup> <http://www.rapid-spr.com/objectives.php?RaSPSESSION=2c84df5355e85dff08b35ec0db8f158a>

### **The RaSP method may become a standard blood screening method**

This diagnostic method represents a revolution in the field of rapid diagnostics. The RaSP method could indeed become a standard method for screening donor blood. Furthermore, other bio-analytical applications are conceivable for this system, such as the detection of emergency markers, food monitoring (detection of food-related pathogens) and monitoring of environmental pathogens and biological warfare agents.

*'The project showed that the RaSP method is feasible. We have solved many individual problems. These solutions are needed as building blocks if a company will take up the RaSP results for building a real product. Examples of such results include new antibodies, new methods for immobilising (printing) antibodies in a defined pattern, concepts and methods for*

*SPR-chip packaging, software and electronics for signal readout and fabrication of metallic nanopatterns. However, RaSP is not a company, it is a project. We cannot produce a diagnostic product and apply for EC mark. Thus there is currently no RaSP product which could be used in routine diagnostic tests,' concludes Dr Velten.*

### **To become a routine diagnostic test, RaSP needs the private sector**

The real exploitation of the project results will have to be done by companies who take up the RaSP results and turn them into real products. One company has already expressed interest in using some of the project results for improving their next generation of SPR products, and another will use RaSP results for future antibody production.



### Further information:

Project website

<http://www.rapid-spr.com/>

<http://www.healthcompetence.eu/converis/publicweb/project/1234?show=Person>

### Project team:

Scientific coordinator:

Dr Thomas Velten

Fraunhofer Institute for Biomedical Engineering (IBMT)

Ensheimer Strasse 48

66386 Sankt Ingbert,

GERMANY

E-mail: [thomas.velten@ibmt.fhg.de](mailto:thomas.velten@ibmt.fhg.de)

### Other principal investigators:

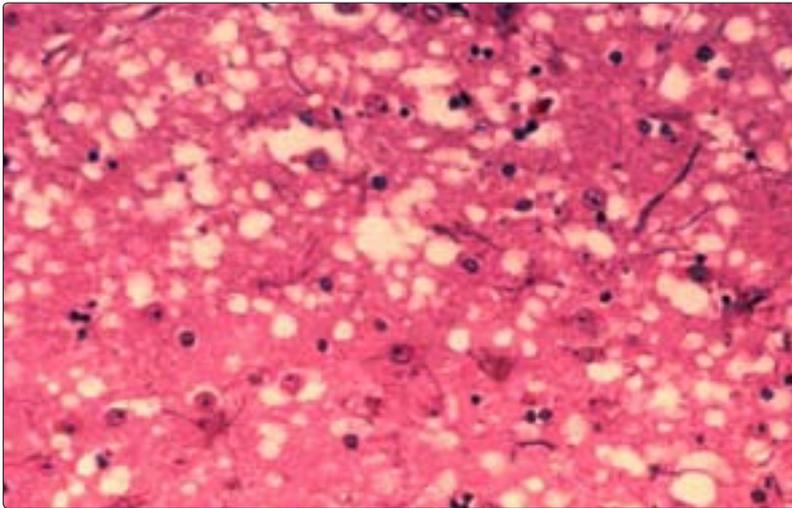
- Hunor Santha (Budapest University of Technology and Electronics)
- Kyle Jiang (The University of Birmingham)
- Vladimir Mirsky (Universitaet Regensburg)
- Waleed Waleed Nazmy El-Mazny (Holding Company for Biological Products and Vaccines (VACSERA))
- Robert Deak (Mikromikomed KFT)
- Alexandre Zybine (Leibniz-Institut Fur Analytische Wissenschaften-ISAS-EV)
- Thomas Hirsch (MIVITEC GMBH)
- Anton Samoylov (Institute of Semiconductor Physics, National Academy of Science of Ukraine)

### EU contribution

This Specific Targeted Research Project has received co-funding from the European Union in the framework of the **6th Research Framework Programme** (FP6-2005-SSP-5-A, Grant: SP5A-CT-2006-044515).

## Development of a Blood Screening Assay for Diagnosis of Prion Diseases in Humans (PRIONSCREEN)

*This Specific Targeted Research Project has received co-funding from the European Union in the framework of the 6<sup>th</sup> Research Framework Programme (FP6-2005-SSP-5-A, Grant: SP5A-CT-2007-044438).*



*The word prion, coined in 1982 by Stanley B. Prusiner, is derived from the words protein and infection. A prion is an infectious agent composed of protein in a misfolded form.*

The word prion, coined in 1982 by Stanley B. Prusiner, is derived from the words protein and infection. A prion is an infectious agent composed of protein in a misfolded form.

This is different from all other known infectious agents (virus/bacteria/fungus/parasite), which contain nucleic acid (either DNA, RNA or both). Prions are responsible for the transmissible spongiform encephalopathies in a variety of mammals, including bovine spongiform encephalopathy (BSE, also known as 'mad cow disease') in cattle and Creutzfeldt-Jakob disease (CJD) in humans. CJD is at times called a human form of mad cow disease even though classic CJD is not related to BSE. However, given that BSE is believed to be the cause of variant Creutzfeldt-Jakob (vCJD) disease in humans, the two are often conflated. Prions do not replicate, they cause other prion proteins to become misfolded. All known prion diseases affect the structure of the brain or other neural tissue and are currently untreatable and universally fatal.

For many decades, CJD was thought to be transmissible among humans only via contact with infectious nervous system tissue. However, recently it was shown that variant Creutzfeldt-Jakob disease (vCJD) can be transmitted by

blood donation<sup>(24)</sup>. The transmission of the disease occurred in the incubation period of the donors, which demonstrates that this route can be highly efficient. Precautionary measures to avoid transmission — such as leucodepletion<sup>(25)</sup> and donor deferral — can be taken. However, these increase the costs of blood and blood products, reduce the donor population and might lead to a shortage of available blood products.

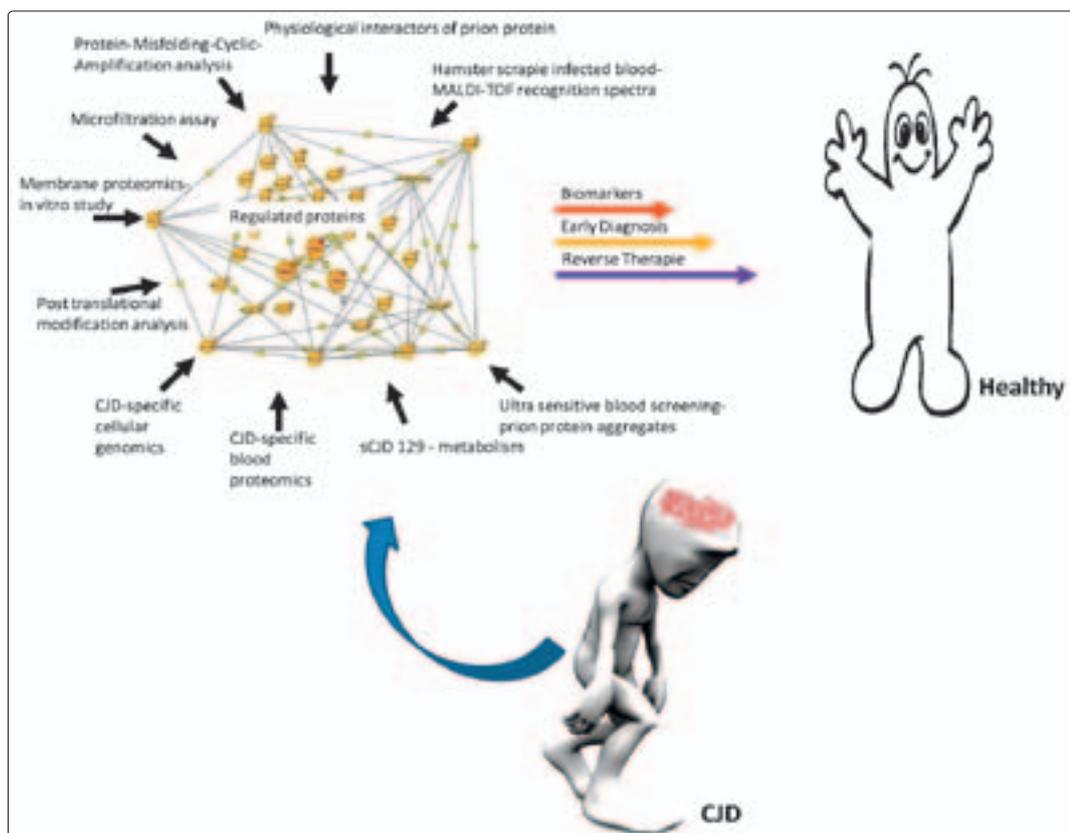
**To reduce public health risks related to undetected infected blood donors, the PRIONSCREEN project was designed**

From a public health perspective, undetected sub-clinically infected blood donors bear a great risk for secondary vCJD transmission, persistence and/or even spread of vCJD epidemic within the human population. Post-mortem brain tissue is currently used to diagnose vCJD. However, a screening method applicable and repeatable in easily accessible tissues and fluids such as blood is urgently required to screen blood donors for abnormal prions at an early stage of infection. Such a method needs to be able to reflect disease pathology in the early stages and therefore be able to indicate a prion infection.

The project PRIONSCREEN, **Development of a blood screening assay for diagnosis of prion diseases in humans**, coordinated by the University of Göttingen and comprising five European partners, was launched in 2007 with a 3-year funding from the Sixth Research Framework Programme (FP6). The

<sup>(24)</sup> However, according to the WHO only four cases of vCJD infection have been associated with blood transfusion: three of these cases developed symptoms of vCJD several years after transfusion, and one died from unrelated causes before developing symptoms of vCJD, but was shown to be infected with vCJD (<http://www.who.int/mediacentre/factsheets/fs180/en/>).

<sup>(25)</sup> Leucodepletion is a process by which leucocytes are removed from donated blood. Leukocytes, or white blood cells, are cells of the immune system involved in defending the body against both infectious disease and foreign materials. The number of leukocytes in the blood is often an indicator of disease.



Graphical representation of a possible outcome of the PRIONSCREEN project.

aim of PRIONSCREEN was to develop easily applicable tests for prion diseases in humans and potentially in animals. Such tests would be more effective for diagnostic purposes and as a screening assay in blood donors.

Since conventional tests require a brain autopsy or biopsy, and surrogate markers often only show positive results in the advanced stages of the disease, the project was set to identify potential biomarkers<sup>(26)</sup> of Creutzfeldt-Jakob disease (CJD) via a blood test using multimodal approaches such as the detection of disease-specific early markers or abnormal protein aggregation. This work was directed towards the identification of specific interacting partners on a protein, mRNA and DNA level.

*'The prion protein that is believed to cause CJD exhibits two isoforms, cellular Prion protein PrP<sup>C</sup> and abnormal PrP<sup>Sc</sup>, which provoke a transmissible spongiform encephalopathy. Recent findings suggest that PrP<sup>C</sup> is a multifunctional*

*protein participating in several cellular processes. Hence, through the project we sought to identify the cellular proteins that specifically interact with PrP<sup>C</sup> and the common genetic variant of Prion protein,'* explains Prof. Dr Inga Kerr, one of the project coordinators.

### After years of research and trials, the project identifies new candidates for diagnostic markers

With several years of research and clinical trials, the team was successful with their unique approaches to identify the novel candidates for diagnostic markers in PrP<sup>C</sup> and in different CJD subtype patient's CSF and blood. Additionally, the project established a well-characterised sample and data banks for infected blood and brain tissue.

The samples are available for further research on biological fluids in patients with CJD and other prion diseases, especially for further test evaluation and harmonisation. The project team also developed microfiltration assays for the detection of prions in the blood of experimentally infected animals and from human tissue samples collected at an early disease stage. *'Importantly, the team characterised the PrP and*

<sup>(26)</sup> A biomarker is a term often used to refer to a protein measured in blood whose concentration reflects the severity or presence of some disease state. More generally a biomarker is anything that can be used as an indicator of a particular disease state or some other physiological state of an organism. A biomarker is often a traceable substance that is introduced into an organism as a means to examine organ function or other aspects of health.

*various PrP isoforms in patients affected by CJD and in controls,' says Prof. Dr Kerr. 'A novel and extremely interesting contribution is the identification of various PrP interacting proteins, which expand our understanding on PrP function in physiological conditions and in disease and will allow better diagnosis and potentially better therapies in future.'*

*“In addition to the scientific outcome of this initiative, the project fostered intense collaborative effort among different European labs. Such collaboration was in itself a remarkable achievement.”*

*Prof. Dr Kerr, project coordinator*

Overall this study has provided valuable new insights in the exploration of the PrP<sup>C</sup> biology and in the establishment of diagnostic assays for PrPdiseases in humans. By performing blood and CSF (cerebrospinal fluid) proteomics (protein analysis) and a functional genomic analysis (gene analysis) of plasma samples from sCJD patients and humanised mice, 49 differentially expressed proteins and a panel of seven dysregulated genes could be identified.

If confirmed by validation studies on a wide number of CJD (including other CJD subtypes) and neurological controls (e.g. Alzheimer's disease, Parkinson disease, Frontotemporal dementia), the CJD-specific plasma proteomic and cellular genomic pattern hold a strong potential for the development of a novel, specific test in an ELISA format to support the *in vivo* diagnosis of CJD.

*'Our results show, for the first time, the occurrence of an apparent CJD-specific alteration of blood physiology and this opens an entirely new line of research to understand the peripheral pathogenesis of this disorder,' concludes Prof. Dr Kerr.*

The research outcome acquired a very positive feedback from scientists all over the world. In addition to the scientific outcome of this initiative, the project fostered intense collaborative effort among different European labs. Such collaboration was in itself a remarkable achievement. Besides the identification and characterisation of novel candidates for diagnostic markers, the project helped to establish further test evaluation and harmonisation of the various protocols amongst the project partners. Further follow-up projects using Prionscreen as a basis are being planned.

### Further information:

Project website

<http://www.prionscreen.de>

[http://ec.europa.eu/research/health/infectious-diseases/emerging-epidemics/projects/161\\_en.html](http://ec.europa.eu/research/health/infectious-diseases/emerging-epidemics/projects/161_en.html)

Health Competence Database:

<http://www.healthcompetence.eu/converis/publicweb/project/1230?show=Person>

### Project team:

Project info:

Prof. Dr Inga Zerr

Prof. Dr Victor Armstrong

Prof. Dr Walter Schulz-Schaeffer

Georg-August University of Göttingen  
Departments of Neurology,  
Clinical Chemistry and Neuropathology  
National Reference Centre for TSE  
Robert-Koch-Str. 40, 37075 Göttingen  
GERMANY

Tel. +49 551396636

Fax +49 551397020

E-mail:

[IngaZerr@med.uni-goettingen.de](mailto:IngaZerr@med.uni-goettingen.de);

[varmstro@med.uni-goettingen.de](mailto:varmstro@med.uni-goettingen.de);

[wjschulz@med.uni-goettingen.de](mailto:wjschulz@med.uni-goettingen.de)

### Other principal investigators:

- Dieter Naumann (Robert Koch-Institut)
- Maurizio Pocchiari (Istituto Superiore di Sanità)
- Cornelia M. van Duijn (Erasmus Medical Centre Rotterdam)
- Eva Judita Mitrová (Slovenska Zdravotnicka Univerzita v Bratislave)
- Michael Bruce Coulthart (Public Health Agency of Canada)
- Alison Green (The University of Edinburgh)

### EU contribution

This Specific Targeted Research Project has received co-funding from the European Union in the framework of the **6th Research Framework Programme** (FP6-2005-SSP-5-A, Grant: SP5A-CT-2007-044438).



# Human tissues and cells for transplantation



The transplantation of human tissues and cells is a strongly expanding field of medicine offering excellent opportunities for the treatment of as yet incurable diseases. Among substances of human origin (SoHO), tissues and cells are the most heterogeneous category, involving both living and deceased donors, and covering various types of tissues/cells, such as:

- replacement tissues, also considered 'traditional' tissues like bone, cartilage and tendons, heart valves and blood vessels, ocular tissues (cornea, sclera) and skin; in the last decade, additional tissues and cells have been added to this category, among them hepatocytes, pancreatic cells and chondrocytes can be mentioned;
- haematopoietic stem cells, which include bone marrow, peripheral blood stem cells, umbilical cord blood stem cells and other stem cells;
- reproductive tissues and cells, which include gametes (sperm, eggs), embryos and testicular/ovarian tissues.

At the EU level, there are approximately 3 700 tissue establishments (TEs) which are involved in the donation, procurement, testing, processing, storage and distribution of this wide variety of tissues and cells. Hundreds of thousands of tissues and cells are procured, and tens of thousands of patients receive such products every year, while other tens of thousands of tissues and cells are preserved and stored for future use.

Presently the EU legislation for tissues and cells includes three Directives: one mother directive, which provides the framework legislation, and two further implementing directives, which provide more detailed requirements for Member States:

- Directive 2004/23/EC of the European Parliament and of the Council on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells;
- Directive 2006/17/EC of the European Parliament and of the Council on certain technical requirements for the donation, procurement and testing of human tissues and cells;

- Directive 2006/86/EC of the European Parliament and of the Council as regards traceability requirements, notification of serious adverse reactions and events and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cells.

These Directives created an EU benchmark for the standards that must be met when carrying out any activity involving tissues and cells for human application.

Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 applies to the donation, procurement, testing, preservation, storage and distribution of human tissues and cells intended for human use. It also relates to manufactured products derived from human tissues and cells intended for human use. In the case of products made industrially from tissues and cells, which within the European Union fall under Regulation 1394/2007 on advanced therapy medicinal products, the Directive applies merely to donation, procurement and testing.

The Directives outline, regarding tissue and cell donation, the following.

- Member States must encourage voluntary and unpaid donations of tissues and cells. However, donors may receive a compensation strictly limited to making good the expenses and inconveniences related to the donation (e.g. travel expenses). Promotion and publicity activities in support of the donation of human tissues and cells with a view to offering or seeking financial gain or comparable advantage are not allowed. The general rule is that Member States must endeavour to ensure that the procurement of tissues and cells is carried out on a non-profit basis.
- The consent of donors, recipients or their next of kin is obligatory. They must receive information on the purpose and nature of the procurement, the associated risks, the analytical examinations, the recording and protection of donor details and medical confidentiality. In case of deceased donors, all this information must be provided to the next of kin and all the necessary authorisations must be obtained from the next of kin before any procurement takes place.

- Member States must take all necessary measures to ensure that all data collected and to which third parties have access are rendered anonymous. Measures must be adopted to ensure data security and prevent unauthorised modifications to files and records.

Ethical considerations do not fall under the scope of these Directives and remain the responsibility of the Member States. In addition, the Directives do not cover research using human tissues and cells (e.g. *in vitro* research

or in animal models) and do not interfere with decisions by Member States on the use or non-use of any specific types of human cells, such as germ cells or embryonic stem cells.

The European Commission has supported the Member States in their efforts to implement the European Tissue and Cells Directives by providing funding for several projects under the EU Health Programmes, but also under various other funding schemes of the European Commission.

## Overview table of projects in this section

Acronym	Title	Page
EUROCET	European registry for organs, tissues and cells project	68
JACIE	Joint Accreditation Committee ISCT Europe and EBMT	72
EUSTITE	European Union standards and training for the inspection of tissues establishments	76
POSEIDON	Promoting optimisation, safety, experience sharing and quality implementation for donation organisation and networking in unrelated haematopoietic stem cell transplantation in Europe	81
Euro-GTPs	European Good Tissue Practices	84
SoHO V&S	Vigilance and Surveillance of Substances of Human Origin	89
EQSTB	European Quality System for Tissue Banking Project	94
Eurocet128	Building reference compendia for the application of a single European coding system for tissues and cells	98
Tiss.EU	Evaluation of legislation and related guidelines on the procurement, storage and transfer of human tissues and cells in the European Union — an evidence-based impact analysis	102
RISSET	Reprogramming the immune system for the establishment of tolerance	107
European LeukemiaNet	Strengthen and develop scientific and technological excellence in research and therapy of leukaemia by integration of the leading national leukaemia networks and their interdisciplinary partner groups in Europe	112
TRIE	Transplantation research integration across Europe	117
	Comparative analysis of medically assisted reproduction in the EU: regulation and technologies	121
	Analysis and comparison of testing methods and testing laboratories in the EU and third countries for the biological markers specified in the blood and tissues and cells Directives	125

## European registry for organs, tissues and cells (EUROCET project)

*This project has received co-funding from the European Union in the framework of the e-TEN programme of the European Commission, DG Communications Networks, Content and Technology (DG CNECT, formerly DG INFSO).*

Achievements in tissue and cell transplantation have improved the results of cures and quality of life for patients suffering from diseases that were incurable before the beginning of transplant medicine. However, concerns about the quality and safety of these substances in the European Union have been rising. In order to regulate this part of medical practice, the European Union issued three Directives<sup>(27)</sup><sup>(28)</sup><sup>(29)</sup>, between 2004 and 2006.

In addition, although donation and transplantation has for long been part of daily medical practice in Europe, there was not a European-wide database which facilitated medical professionals to find organs, tissues and cells for transplant patients. Each Member State maintained national registries, but an overall integrated information and communication system across the European Union was lacking. And it was clear that the centralisation of this information could significantly improve the quality and safety of organ donation and transplantation. This is the background in which EUROCET was born.

The EUROCET project was funded by the European Union under its e-TEN programme (e-TEN stands for trans-European e-services programme, which finished at the end of 2006 and provided funds to make e-services available throughout the European Union<sup>(30)</sup>). The EUROCET project was coordinated by the Istituto Superiore di Sanità (Italy) and lasted

18 months, starting on September 2005 and finishing on February 2007. It involved a consortium created by 20 partners coming from the following EU Member States: Italy, France, Spain, the United Kingdom, Belgium, the Netherlands, Germany, Slovenia, Hungary, Poland, the Czech Republic, Slovakia and Estonia.

As the EUROCET team highlighted<sup>(31)</sup>, the project was built on the successes of EURODONOR (European donors and organs registry), a previous project which created a registry on organ donation and transplantation activity in the old EU Member States (Belgium, Greece, Italy, Netherlands, Spain and the United Kingdom). EURODONOR could be seen as the 'mother project'. As EUROCET was launched in 2005, it was able to be extended to six new Member States (the Czech Republic, Estonia, Hungary, Poland, Slovakia and Slovenia).

### EUROCET created a registry shared by Member States

What did the EUROCET project seek? The goal was to create a common registry shared by both old and new Member States for the data collection on organ, tissue and cell donation and transplantation activity. The EUROCET registry was designed to support the collection and analysis of data supplied by the participating countries, as well as the delivery of information to the professional users and citizens<sup>(31)</sup>.

Coordinated by the Italian National Transplant Centre (Rome), the registry represented the realities of different Member States, with the following key objectives:

- standardise methodologies for data collection and processing;
- share knowledge in this field;
- strengthen the cooperation and delivery of official and updated information.

<sup>(27)</sup> Directive 2004/23/EC — 'Setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells'.

<sup>(28)</sup> Directive 2006/17/EC — 'Implementing Directive 2004/23/EC of the European Parliament and of the Council as regards certain technical requirements for the donation, procurement and testing of human tissues and cells'.

<sup>(29)</sup> Directive 2006/86/EC — 'Implementing Directive 2004/23/EC of the European Parliament and of the Council as regards traceability requirements, notification of serious adverse reactions and events and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cells'.

<sup>(30)</sup> [http://ec.europa.eu/information\\_society/activities/eten/index\\_en.htm](http://ec.europa.eu/information_society/activities/eten/index_en.htm)

<sup>(31)</sup> [www.eurocet.org](http://www.eurocet.org)

Nowadays, the registry remains active as an online system. Data suppliers can use a file transfer at a dedicated e-mail address (eurocet@iss.it) or can access the EURO CET system with a user identification, which ensures that only authorised users transmit official information to the database. Moreover, information provided has to be compliant with the national regulations regarding privacy and data protection: ‘all data collected is therefore aggregated data or individual anonymous data, which does not require specific security agreements or protection’<sup>(32)</sup>.

The registry represents a central repository of validated and updated information on organ, tissue and cell donation and transplantation activity across Member States.

### From the EURO CET project to the EURO CET Network

Even though EURO CET finished in February 2007, this has not signified the end of EURO CET.

EURO CET has evolved from a project to a network which supports the collection and analysis of data supplied by the participating countries, as well as the delivery of information to the professional users and citizens. Since 2008 the Italian National Transplant Centre (Rome) is in charge of coordinating the EURO CET network. Today EURO CET hosts the following.

#### 1. The European Registry of the Competent Authorities for tissues and cells<sup>(33)</sup>

The EURO CET network maintains an accessible and updated register of Competent Authorities across Europe. In the field of tissues and cells for human application (including haematopoietic cells, gametes and embryos), the **Competent Authorities** are organisations designated by each Member State as required by Directive 2004/23/EC. The EURO CET network goes beyond the then 27 EU Member States, currently including 34 countries. Because Member States and non-EU countries can have more than one Competent Authority for tissues and cells, a total of 59 Competent Authorities are recorded in EURO CET<sup>(33)</sup>.

“ *The European Union encourages the use of the EURO CET portal to fulfil some of the obligations of the tissues and cells directives.* ”

#### 2. The registry of tissue establishments coming from all Competent Authorities

Tissue establishments are authorised centres that receive, test, process, store and distribute tissues or cells (including gametes and embryos) for human application in the European Union. EURO CET responds to the requirements of the EU Directives by publishing an updated registry of all tissues establishments in the European Union<sup>(34)</sup>. Presently there are more than 4 500 establishments recorded<sup>(35)</sup>.

#### 3. Data regarding tissues and cells’ donation and transplantation provided by all national Competent Authorities

Nowadays, data on donation and transplantation are reported by the Competent Authorities to EURO CET on a voluntary basis<sup>(36)</sup>. These data are periodically published in the ‘International Figures on Donation and Transplantation’<sup>(37)</sup>.

#### 4. An instrument which provides a standard terminology for organs, tissues and cells

A glossary was agreed among the European countries involved in the EURO CET project with the objective of harmonising the terminology used in the field of organ, cell and tissue donation and transplantation. This glossary is available on the EURO CET website<sup>(31)</sup>.

### EURO CET — an important website for donation and transplantation activities

EURO CET has become a valuable website (www.eurocet.org) in the European Union for all citizens, patients, professional operators and institutions interested in organs, tissues and cells donation and transplantation activities<sup>(31)</sup>. Both EU and international professional operators and institutions can rely on the complete

<sup>(34)</sup> [www.iss.it/ecet/tiss/index.php?lang=2&tipo=18&anno=2009](http://www.iss.it/ecet/tiss/index.php?lang=2&tipo=18&anno=2009)

<sup>(35)</sup> [www.ncbi.nlm.nih.gov/pmc/articles/PMC3267997/pdf/trmh0038-0352.pdf](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3267997/pdf/trmh0038-0352.pdf)

<sup>(36)</sup> [www.iss.it/ecet/dati/index.php?lang=2&tipo=12&anno=2009](http://www.iss.it/ecet/dati/index.php?lang=2&tipo=12&anno=2009)

<sup>(37)</sup> Council of Europe: International figures on donation and transplantation — 2010. Newsletter Transplant 2011;16:47–58.

<sup>(32)</sup> [http://ec.europa.eu/information\\_society/activities/eten/cf/opdb/cf/project/index.cfm?mode=desc&project\\_ref=ETEN-517417](http://ec.europa.eu/information_society/activities/eten/cf/opdb/cf/project/index.cfm?mode=desc&project_ref=ETEN-517417)

<sup>(33)</sup> [www.iss.it/ecet/scie/index.php?lang=2&tipo=23&anno=2009](http://www.iss.it/ecet/scie/index.php?lang=2&tipo=23&anno=2009)

and updated databases of the EURO CET website. According to the EURO CET team, this has turned to be a popular channel to increase public awareness and sensibility towards the value of donation<sup>(35)</sup>. In this sense, the website has proved to be a powerful tool for communication and dissemination.

The use of the EURO CET portal has been encouraged by the European Union as a way to fulfil some of the obligations of the tissues and cells directives<sup>(35)</sup>. This reflects the important work EURO CET is performing in order to contribute to the setting of standards of quality and safety in the field of organ, tissue and cell donation and transplantation in Europe.

For more information about the EURO CET Network, see 'The EURO CET Network: Support for Coding, Vigilance and Surveillance'<sup>(35)</sup>.



### Further information:

EC DG CNECT Project Factsheet:

[http://ec.europa.eu/information\\_society/activities/eten/cf/opdb/cf/project/index.cfm?mode=detail&project\\_ref=ETEN-517417](http://ec.europa.eu/information_society/activities/eten/cf/opdb/cf/project/index.cfm?mode=detail&project_ref=ETEN-517417)

Project website

<http://www.eurocet.org/>

### Project team:

Project leader:

Italian National Transplant Centre

Istituto Superiore di Sanità

Viale Regina Elena 299

00161 Rome RM

ITALY

Tel. +39 0649904040-1

Fax +39 0649904101

E-mail: [eurocet@iss.it](mailto:eurocet@iss.it)

### Associated partners:

- Sihtasutus Tartu Ulikooli Kliinikum, Estonia
- Agence de la Biomédecine, France
- Hungarotransplant Egeszsegugyi Koordinalo Kozhasznu Tarsasag, Hungary
- Finsiel — Consulenza e Applicazioni Informatiche S.P.A., Italy
- Istituti Ortopedici Rizzoli, Italy
- Eutelis Consult Italia & Associates — S.R.L., Italy
- Stichting Donor Action Foundation, Netherlands
- Stichting Bio Implant Services, Netherlands
- Stichting Eurotransplant International Foundation, Netherlands
- Centrum Organizacyjno-Koordynacyjnego do Spraw Transplantacji Poltransplant, Poland
- Wroclaw Medical University, Poland
- Artman Technologies S.R.O., Slovakia
- University Hospital Martin, Slovakia
- Zavod Republike Slovenije Za Presaditve Organov in Tkiv Slovenija Transplant, Slovenia
- Fundacio Bosch i Gimpera, Spain
- Organizacion Nacional de Trasplantes, Spain
- Fundacio Privada Transplant Services Foundation, Spain
- United Kingdom Transplant, United Kingdom
- Transplantations Coordinating Centre, Czech Republic

### EU contribution

This project has received co-funding from the European Union in the framework of the **e-TEN programme of the European Commission, DG CNECT**.

## Joint Accreditation Committee ISCT Europe & EBMT (JACIE)

*This project has received co-funding from the European Union in the framework of the Public Health Programme 2003–2008 (Grant: 2003208).*

JACIE<sup>(38)</sup> stands for the Joint Accreditation Committee ISCT Europe & EBMT. In turn, ISCT stands for the International Society for Cellular Therapy<sup>(39)</sup>, and EBMT for the European Group for Blood and Marrow Transplantation<sup>(40)</sup>. JACIE is a non-profit body established in 1998 for the purposes of assessment and accreditation in the field of haematopoietic stem cell transplantation.

The JACIE accreditation programme was funded in 2004 by the European Union under its Public Health Programme. The project was coordinated by Fiona Mc Donald, who was the Executive Officer of EBMT at that time. During 14 months, from January 2004 to February 2005, partners from six Member States (Belgium, France, Netherlands, Spain, Sweden, and the United Kingdom) worked together with the same aim: to provide vital impetus to the JACIE programme and to ensure its integral role in the setting of standards, inspection and

accreditation for establishments involved in haematopoietic stem cell collection, processing and transplantation in Europe.

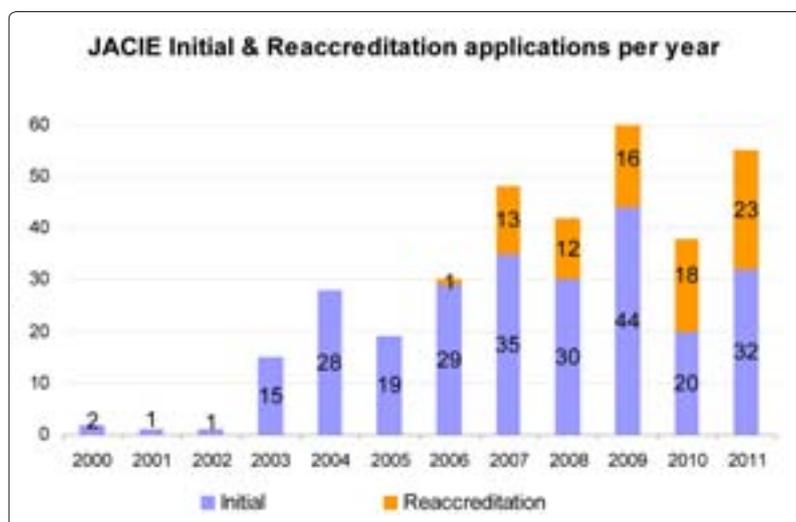
The EU-funded project aimed at promoting high-quality patient care and laboratory performance in centres dedicated to haematopoietic stem cell collection, processing and transplantation through an internationally recognised system of accreditation.

### What is haematopoietic stem cell transplantation and why is the JACIE accreditation programme important in this field?

Tissues and organs in the body are made of specialised cells that assure their specific functions. Maintenance and repair of these tissues and organs depend upon resident unspecialised adult stem cells, which are still at an early stage of development and retain the potential to turn into the different types of cells of a particular tissue or organ. In the bones, the haematopoietic stem cells give rise to all kinds of blood cells<sup>(41)</sup>. For this reason, the haematopoietic stem cell transplantation, often performed for patients with certain blood cancers, such as leukaemia, is considered one of the most important medical advances in the second half of the 20th century.

Accreditation of a centre is the process which certifies its competency. In this sense, a centre accredited by JACIE demonstrates that it is performing its functions according to quality standards. In cells transplant programmes, this accreditation certifies that the clinical, collection and laboratory units are all working together to achieve excellent practices and increased guarantees for patients. And this is important because working according to quality standards benefits transplant patients<sup>(42)</sup>.

“The JACIE project is considered an example of how EU funding can facilitate the harmonisation, implementation and use of common standards.”<sup>(42)</sup>



JACIE Annual Report 2011 (<http://www.jacie.org/about/annual-report>)

<sup>(38)</sup> [www.jacie.org](http://www.jacie.org)

<sup>(39)</sup> [www.celltherapysociety.org](http://www.celltherapysociety.org)

<sup>(40)</sup> [www.ebmt.org](http://www.ebmt.org)

<sup>(41)</sup> [http://ec.europa.eu/research/fp6/index\\_en.cfm?p=1\\_stem\\_home](http://ec.europa.eu/research/fp6/index_en.cfm?p=1_stem_home)

<sup>(42)</sup> [www.jacie.org/about](http://www.jacie.org/about)

## The JACIE project provided concrete input to the EU Directive on standards for the quality and safety of human tissue and cells

The EU-funded project produced a new edition (the second edition at that time) of the JACIE's Standards and of the JACIE's Accreditation Manual, both in line with the EU Directive of human tissues and cells<sup>(43)</sup>. According to the project team, JACIE achieved a great distribution of this manual, as 83 % of active transplant centres in Europe at that moment received copies of it. By doing so, JACIE offered Member States a set of standards and a programme of accreditation fulfilling the EU requirements. Therefore, JACIE contributed to harmonise healthcare facilities involved in haematopoietic stem cell collection, processing and transplantation across Europe<sup>(44)</sup>. Nowadays, the 5th edition of the Standards and the Accreditation Manual, published in March 2012, are available on the JACIE website<sup>(45)</sup>.

Another objective of the project was to provide vital impetus to the implementation of the JACIE accreditation programme in a core number of centres in Europe. In order to facilitate this, the European JACIE Office was established in Barcelona. This reinforcement of the central resources proved to be fundamental to enhance effectiveness of the existing JACIE network.

Furthermore, an effective online system, JACIE Online<sup>(46)</sup>, was developed. This online tool offers all steps, from the beginning until the end, that a centre must follow when it applies for its accreditation. Therefore, the tool facilitates the collection, tracking and monitoring of information on the implementation of the JACIE accreditation. According to the project team, during the project '18 out of the 19 countries within the current JACIE network had accepted to administer the JACIE accreditation process via the online system'. This tool has increased the comparability of data across Member States<sup>(44)</sup>.

<sup>(43)</sup> Directive 2004/23/EC — 'Setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells'.

<sup>(44)</sup> Final Technical Implementation Report Grant agreement No 2003208 Action: JACIE.

<sup>(45)</sup> [www.jacie.org/standards](http://www.jacie.org/standards)

<sup>(46)</sup> [www.jacie.org/news/onlinesystemforaccreditations](http://www.jacie.org/news/onlinesystemforaccreditations)

## INTERNATIONAL STANDARDS FOR CELLULAR THERAPY PRODUCT COLLECTION, PROCESSING, AND ADMINISTRATION



Fifth Edition  
Version 5.3  
March 2012

### NOTICE

These Standards are designed to provide minimum guidelines for programs, facilities, and individuals performing cell transplantation and therapy or providing support services for such procedures. These Standards are not intended to establish best practices or include all procedures and practices that a program, facility, or individual should implement if the standard of practice in the community or applicable governmental laws or regulations establish additional requirements. Each program, facility, and individual should analyze its practices and procedures to determine whether additional standards apply. Compliance with these Standards is not an exclusive means of complying with the standard of care in the industry or community or with local, national, or international laws or regulations.

The Foundation for the Accreditation of Cellular Therapy and the Joint Accreditation Committee - ISCT and EBMT expressly disclaim any responsibility for setting maximum standards and further expressly disclaim any responsibility, liability, or duty to member programs, directors, staff, or program donors or patients for any such liability arising out of injury or loss to any person by the failure of member programs, directors, or staff to adhere to the Standards or related guidance.

COPYRIGHT © 2012  
FOUNDATION FOR THE ACCREDITATION  
OF CELLULAR THERAPY (FACT)

COPYRIGHT © 2012  
JOINT ACCREDITATION COMMITTEE -  
ISCT and EBMT (JACIE)

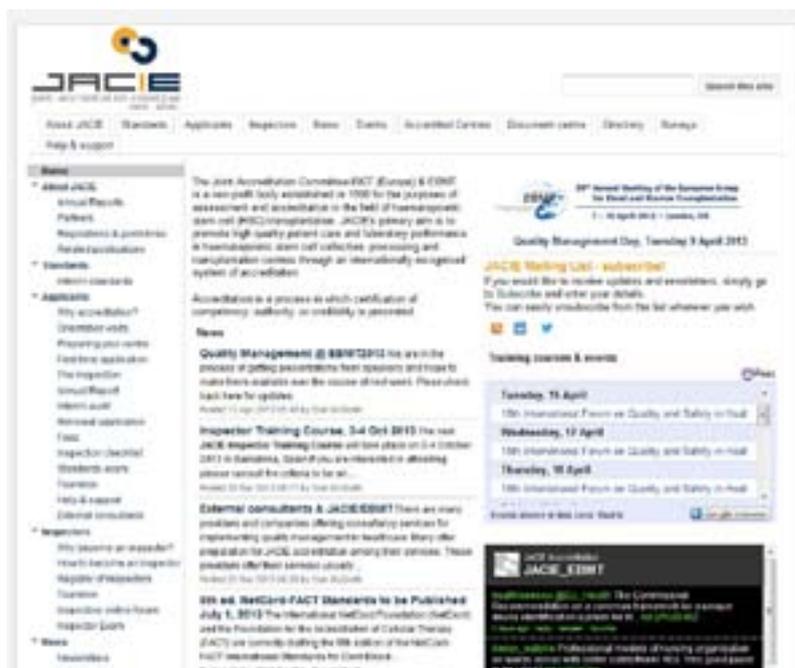
JACIE Accreditation Manual <sup>(47)</sup>

“The project demonstrated that the accreditation process is viable and has the full support of professionals.”<sup>(44)</sup>

Another achievement of the JACIE project in 2004 was the development of programmes and training materials for two types of training courses:

- a course in preparing a quality management system according to JACIE standards;
- an inspector training course, which was designed to prepare healthcare professionals to carry out inspections in transplant centres.

<sup>(47)</sup> <http://www.jacie.org/standards>



JACIE webpage <sup>(48)</sup>

During 2004, four courses were held on these issues and were attended by a total of 105 professionals from across Europe. According to the final report of the project, 'these professionals came from different backgrounds (clinical, collection and processing) and the courses proved an excellent opportunity for sharing of best practice between different disciplines and countries.' The courses were evaluated and rated as highly satisfactory<sup>(44)</sup>.

As stated by the final report of the project, 'common training courses and exams should help to ensure that the JACIE accreditation programme is applied with equal rigour throughout Europe and thereby contribute to the overall harmonisation of standards and systems of accreditation'<sup>(44)</sup>.

The best materials obtained from the training courses were compiled into a consolidated document, which turned out to be of great value to facilities that were considering to apply for or were in the process of applying for a JACIE accreditation and did not know where to start. The document illustrated how other facilities had approached the JACIE accreditation process; therefore it provided a good basis to start working with.

During the project period, 25 inspections were conducted in health institutions and facilities, and eight new countries joined the JACIE network. Although the JACIE accreditation process supposed a considerable strain on resources for the majority of participating centres, these centres felt the effort was worthwhile and that their programmes had benefited from the process. The project team considered vital the confidence of participating centres in the benefits of the JACIE accreditation process, as this would be decisive for the promotion and future success of the JACIE accreditation programme<sup>(44)</sup>.

According to several surveys completed during the project, there was an important need for training clinical staff (doctors and nurses) in quality management as well as for improving the quality management culture in the clinical setting. Therefore, JACIE defined this area as a relevant one for the coming years, and considered that educational material about quality management in the transplant centres should be provided<sup>(44)</sup>.

The list with information on the accreditation status of all centres currently participating in the JACIE programme can be consulted online<sup>(49)</sup>. This list is regularly updated with centres that have received accreditation. The increasing number of accredited centres indicates the potential impact of projects like JACIE.

JACIE was recently highlighted as an exemplary project in a 2011 review of EU funded projects: 'It is also outstanding in its continuing activities after the end of the project period and its success with regard to international collaboration and contribution to public health policies and regulation'<sup>(50)</sup>.

<sup>(48)</sup> [www.jacie.org/accredited-centres](http://www.jacie.org/accredited-centres)

<sup>(50)</sup> [http://ec.europa.eu/health/programme/docs/ex\\_post\\_evaluation\\_en.pdf](http://ec.europa.eu/health/programme/docs/ex_post_evaluation_en.pdf)

<sup>(48)</sup> <http://www.jacie.org/>



### Further information:

Project website

<http://www.jacie.org>

<http://ec.europa.eu/eahc/projects/database.html?prjno=2003208>

### Project team:

European Group for Blood and Marrow Transplantation

P. Debyelaan 25

PO-BOX

6229 HX Maastricht

NETHERLANDS

Tel. +34 934549543

Fax +34 934531263

### Associated partners:

- Belgian Haematological Society, Belgium
- Société française de greffe de moelle et de thérapie cellulaire, France
- Dutch National Registry, Netherlands
- Spanish Group for Haematopoietic Transplantation, Spain
- Swedish Society of Haematology, Sweden
- British Society of Blood and Marrow Transplantation, United Kingdom

### EU contribution

This project has received co-funding from the European Union in the framework of the **Public Health Programme 2003–2008** (Grant: 2003208).

Maximum EC contribution:

EUR 167 526.13

## European Union standards and training for the inspection of tissues establishments (EUSTITE)

*This project has received co-funding from the European Union in the framework of the Public Health Programme 2003–2008 (Grant: 2005204).*

EUSTITE stands for European Union standards and training for the inspection of tissues establishments. EUSTITE was a multinational project funded by the European Union under its Public Health Programme. It lasted 3 years, from December 2006 to December 2009. The project was coordinated by the Italian National Transplant Centre (Rome) and brought together partners from 11 organisations coming from 10 different Member States (Austria, Bulgaria, Denmark, France, Ireland, Italy, Poland, Spain, Slovakia and the United Kingdom). The World Health Organisation (WHO) also participated in the project.

EUSTITE aimed to support the implementation of three European Union Directives<sup>(51)</sup><sup>(52)</sup><sup>(53)</sup> which require all Member States to take regulatory actions to ensure the appropriate quality and safety of tissues and cells for transplantation and assisted reproduction. This applies to tissues for transplantation (such as corneas, heart valves, bone and skin), to haematopoietic stem cells and to cells used in fertility treatments.

According to these Directives, each Member State has to designate at least one Competent Authority responsible, among others, for the following aspects:

- inspecting and certifying tissue and cell procurement;
- inspecting and certifying the centers (referred to as tissue establishments) where these tissues and cells are processed or stored;

- putting vigilance systems in place, in order to report serious adverse events and serious adverse reactions in the field of transplantation and assisted reproduction.

When EUSTITE was conceived, most EU Member States had recently implemented or were planning to implement systems for the inspection and certification of tissue establishments, and were starting to put vigilance systems in place. At that time, there was a wide variation regarding the approaches being taken and the stage of development of these initiatives in Europe. For this reason, EUSTITE attempted to provide guidance in inspection and vigilance, in order to promote their standardisation across Member States.

### EUSTITE attempted to develop common guidelines for inspection and vigilance

EUSTITE aimed to promote standardisation across Member States to best practice in compliance with the tissues and cells Directives. The specific project objectives were the following.

- **Inspection:** To promote standardisation in the inspection of tissue establishments, by providing high quality guidelines for the conduct of inspections and by standardising the training for inspectors.
- **Vigilance:** To develop common tools and guidance for implementation of vigilance systems of adverse events and adverse reactions related to tissues and cells for human application. This system may be used in the future as a European or a global model for vigilance and surveillance. With this aim, the WHO was included as a partner in recognition of the need to consider vigilance in the global context.

The partners in the consortium were selected to represent the scope and level of development regarding the inspection activity of tissue establishments in the European Union. With this aim, organisations both with and without experience to that date were included. Other

<sup>(51)</sup> Directive 2004/23/EC — 'Setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells'.

<sup>(52)</sup> Directive 2006/17/EC — 'Implementing Directive 2004/23/EC of the European Parliament and of the Council as regards certain technical requirements for the donation, procurement and testing of human tissues and cells'.

<sup>(53)</sup> Directive 2006/86/EC — 'Implementing Directive 2004/23/EC of the European Parliament and of the Council as regards traceability requirements, notification of serious adverse reactions and events and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cells'.

relevant organisations collaborated with the consortium, although not as partners; this was the case of the Pharmaceutical Inspectorate Cooperation Scheme (PICS), the European Association of Tissue Banks (EATB) or JACIE<sup>(54)</sup>.

## What were the main outputs of the EUSTITE project?

### 1. Inspection of tissue and cell procurement and tissue establishment (Guidelines for Competent Authorities)<sup>(55)</sup>

According to EUSTITE, a first edition of the guidelines was developed by a drafting group following a review of existing national documents and guidance in related fields. A second edition was developed, incorporating inputs from various project activities which had highlighted good practice in the field. Finally, the guidelines were the subject of an open consultation<sup>(56)</sup>.

The final version of the guidelines proposed <sup>(56)</sup>:

- qualifications and training of inspectors: education and experience, initial training, specialised training, certification and continuous development, and responsibilities, among other issues;
- inspection scheduling: prioritisation for the scheduling of routine inspections; planification of additional (non-routine) inspections;
- different types of inspection;
- how to conduct an inspection;
- formats for the collection of information prior to inspections and the reporting of inspections.

According to the evaluations performed during the project, the guidelines were considered as a high-quality document, very useful and



*EUSTITE, Deliverable 18, Inspection Guidelines, Edition II*

in line with the European legislation, so they would be practically applicable across the EU, although some adaptations should be considered in countries with an inspection system already in place<sup>(57)</sup>.

The European Union used the EUSTITE Inspection Guidelines as the basis for developing the Operational Manual for Competent Authorities for Tissues and Cells in the EU <sup>(58)</sup><sup>(59)</sup>. Therefore, the EUSTITE work clearly achieved the goal of supporting Member States that were establishing such regulatory systems for the

<sup>(54)</sup> JACIE ([www.jacie.org](http://www.jacie.org)) is a non-profit body whose primary aim is to promote high-quality patient care and laboratory performance in haematopoietic stem cell collection, processing and transplantation centres through an internationally recognised system of accreditation.

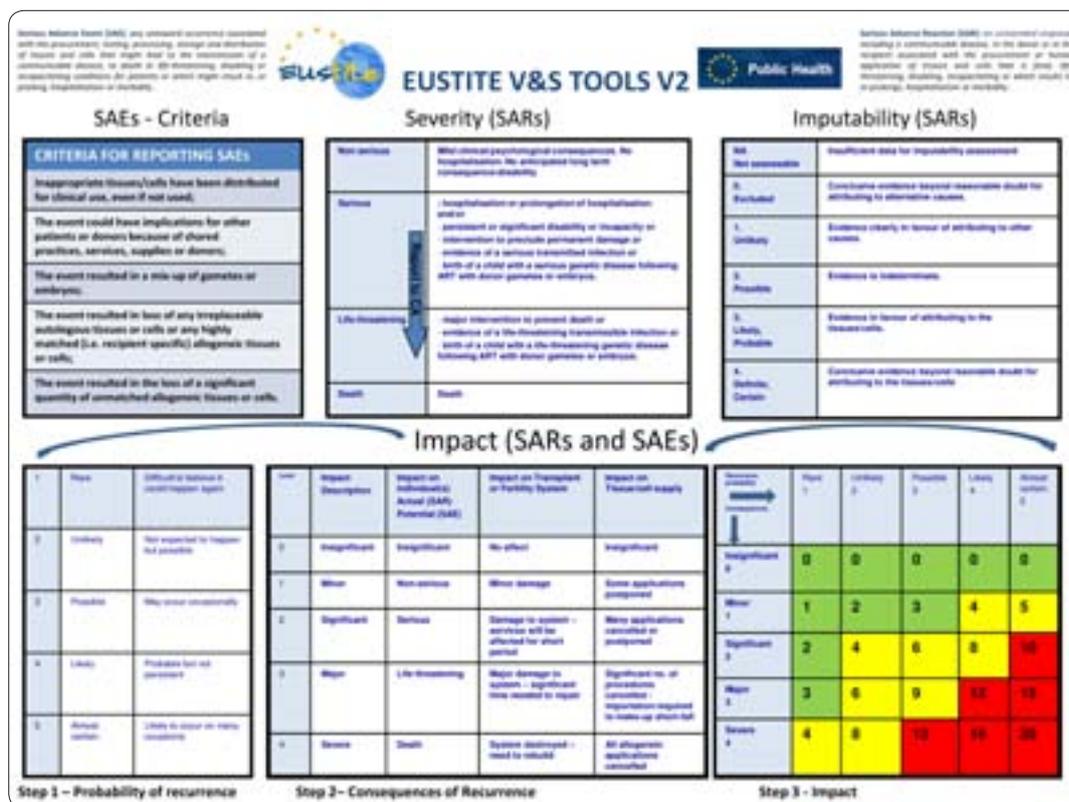
<sup>(55)</sup> Project EUSTITE, Deliverable 18, Inspection of tissue and cell procurement and tissue establishment (Guidelines for Competent Authorities), Second edition, May 2008.

<sup>(56)</sup> Fehily D, et al. *Organs, tissues and cells* 2008; (3): 167-74.

<sup>(57)</sup> Project EUSTITE, Deliverable 8, Final project evaluation report.

<sup>(58)</sup> <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32010D0453:EN:NOT>

<sup>(59)</sup> [http://ec.europa.eu/health/blood\\_tissues\\_organs/docs/manual\\_en.pdf](http://ec.europa.eu/health/blood_tissues_organs/docs/manual_en.pdf)



EUSTITE Vigilance Documents (<http://www.sohovs.org/soho/mod/resource/view.php?id=43>)

first time. Furthermore, it also promoted the standardisation of regulatory systems that were already well established.

## 69 participants from 28 European countries were trained in these guidelines

### 2. The training courses for inspectors of tissue establishments

EUSTITE designed a training programme for inspectors in order to capacitate them according to the EU Directives and to the EUSTITE guidelines on inspection. The programme comprised four courses that took place between June 2008 and July 2009. Each course was divided in two parts: 6 weeks of e-learning via the Internet, and a 3-day residential course, which was held in Vienna, Sofia, Copenhagen and Como.

According to the project team, 'the courses included 69 participants originating from 28 European countries'. Furthermore, after a thorough evaluation, it was concluded that the training programme was well appreciated by the participants, the tutors and the guest observers. For example, the courses were defined as

'excellent' by 42 of the 69 participants. Most of them highlighted that the courses were very interesting, relevant and practically applicable. In short, the model seemed to be a very useful tool for the training of inspectors<sup>(57)</sup>.

### 3. Vigilance and surveillance tools and guidance for tissues and cells used in transplantation or assisted reproduction

In the European Union context in which EUSTITE was planned, Member States were attempting to follow the requirements of the Directives on tissues and cells. In order to do so, they were actively designing and implementing systems for the notification and management of adverse events and reactions associated with tissues and cells used in transplantation or assisted reproduction, that is, vigilance and surveillance systems.

Vigilance and surveillance systems include ongoing data collection, analysis to convert this data into statistics, interpretation of this analysis to produce information and dissemination of this information to those who can take appropriate action<sup>(60)</sup>. However, guidance on what should

<sup>(60)</sup> [http://ecdc.europa.eu/en/healthtopics/spotlight/spotlight\\_surveillance/Pages/Key\\_message\\_1.aspx](http://ecdc.europa.eu/en/healthtopics/spotlight/spotlight_surveillance/Pages/Key_message_1.aspx)

be reported, how it should be classified, when it should be shared nationally or internationally and how it should be managed was not available at that time for vigilance and surveillance in the field of tissues and cells used in transplantation and assisted reproduction. In this sense, it was possible that a Member State developed independent systems on its own that later found to be incompatible with other systems in the European Union. This would finally cause that important safety and quality information was not shared effectively among countries.

EUSTITE constituted a group of experts to review the existing systems in Member States and globally for vigilance and surveillance in the field of tissues and cells used in transplantation and assisted reproduction. The WHO chaired this task in recognition of the need to consider vigilance in the global context<sup>(61)</sup>.

The aim was to identify systems being used at that time in Member States or elsewhere that could be useful to other states which were still developing their system. This working group also identified commonalities in approaches to vigilance and surveillance systems between Member States which would allow a better basis for a common European reporting system.

Finally, tools and guidance for evaluation and management of serious adverse events and reactions associated with tissues and cells were developed and tested during a 1-year pilot phase (from 1 July 2008 to 30 June 2009) involving 20 Member States. This pilot phase attempted to evaluate the applicability of the tools and to help their improvement before final submission to the European Commission<sup>(62)</sup>.

According to Stephanie Sullivan, the pilot coordinator, *'the pilot demonstrated the feasibility of multinational cooperation in vigilance and surveillance in the area of tissue and cells for human application. The tools developed during the EUSTITE project were tested in multiple countries on a large number of real serious adverse reactions and serious adverse events and were found to be easily applied by Competent Authorities vigilance officers, although some reservations were expressed in relation to their direct applicability in the field of assisted reproduction'*<sup>(62)</sup>.

A final document with tools and guidance for vigilance and surveillance in tissues and cells was generated. It provided tools for the definition, classification and evaluation as well as notification and management of serious adverse reactions and serious adverse events within and between EU Member States. These criteria were incorporated into the guidance provided to Member States for the completion of their annual vigilance reports to the European Union<sup>(63)</sup><sup>(64)</sup>.

### EUSTITE Vigilance & Surveillance final recommendations

A number of general recommendations for improving vigilance and surveillance for tissues and cells were made to the European Union. In addition, EUSTITE highlighted a number of areas for further work, particularly the need for:

- investigation guidance;
- training;
- guidance for vigilance in assisted reproduction;
- guidance for the investigation of illegal and fraudulent activity;
- a greater engagement of clinicians to ensure effective vigilance.

These issues are now being taken forward in a new EU-funded project, SoHO V&S, which stands for Vigilance and Surveillance of Substances of Human Origin, a project also coordinated by the Italian National Transplant Centre. Started in March 2010, this new project will continue to contribute to the implementation of the tissues and cells Directives in the European Union.

<sup>(61)</sup> Project EUSTITE, Review of vigilance and surveillance systems for tissues and cells.

<sup>(62)</sup> Project EUSTITE, Deliverable 11b, Vigilance and Surveillance EUSTITE Pilot Report.

<sup>(63)</sup> [www.sohovs.org/soho](http://www.sohovs.org/soho)

<sup>(64)</sup> [www.organsandtissues.net/index.php?id=91&tx\\_ttnews\[tt\\_news\]=574&cHash=08c5f51e0fa89fef161d5e403844e55](http://www.organsandtissues.net/index.php?id=91&tx_ttnews[tt_news]=574&cHash=08c5f51e0fa89fef161d5e403844e55)



### Further information:

Project website

<http://ec.europa.eu/eahc/projects/database.html?prjno=2005204>

<http://www.sohovs.org/soho/mod/resource/view.php?id=43>

### Project team:

Instituto Superiore di Sanità — Centro Nazionale Trapianti

Viale regina Elena 299

PO-BOX

00161 Rome RM

ITALY

Tel: +39 0649901

Fax +39 0649387118

Project leader:

Alessandro Nanni Costa

E-mail: [cnt@iss.it](mailto:cnt@iss.it)

### Associated partners:

- Bundesministerium für Gesundheit und Frauen, Austria
- Organización Nacional de Trasplante, Spain
- Agence de la Biomédecine, France
- Fakultna Nemocnica s Poliklinikou Bratislava — University Hospital Bratislava, Slovakia
- Krajowe centrum Bankowania Tkanek i Komórek (National Centre of Tissue and Cell Banking), Poland
- Laegemiddelstyrelsen (Danish Medicines Agency), Denmark
- Irish Medicines board, Ireland
- Executive Agency for Transplantation, Bulgaria
- Human fertilisation and Embriology Authority, United Kingdom
- Agence Française de Sécurité sanitaire des Produits de Santé, France
- World Health Organisation, Switzerland

### EU contribution

This project has received co-funding from the European Union in the framework of the **Public Health Programme 2003–2008** (Grant: 2005204).

## Promoting optimisation, safety, experience sharing and quality implementation for donation organisation and networking in unrelated haematopoietic stem cell transplantation in Europe (POSEIDON)

*This project has received co-funding from the European Union in the framework of the Public Health Programme 2003–2008 (Grant: 2006210).*

Haematopoietic stem cells (HSC) are immature cells that retain the potential to turn into the different types of blood cells. HSC are often transplanted to patients with malignant (leukaemia, lymphoma, etc.) or non-malignant haematological disorders (inherited disorders, autoimmune diseases, etc.), in order to rebuild the body's immunity or capacity to produce blood cells. This is a process known as haematopoietic stem cells transplantation (HSCT).

HSC mostly live in the 'bone marrow' (located in the centre of certain bones), dividing themselves to produce blood cells. Once blood cells are mature they leave the bone to enter the bloodstream. However, a small number of HSC also get into the bloodstream, where they are called 'peripheral blood stem cells' (PBSC)<sup>(65)</sup>. Finally, HSC are also present in the foetal blood remaining in the umbilical cord after delivery. Therefore, HSC can be collected from the bone marrow, the bloodstream or the umbilical cord to be transplanted.

### Only a third of patients requiring haematopoietic stem cells transplantation have a suitable family donor

HSCT saves lives. However, only a third of patients requiring HSCT have a compatible family donor, so HSC must be obtained from unrelated compatible donors.

There are two main sources to obtain unrelated HSC: the registries of volunteer donors (for bone marrow and PBSC) and banks of cord blood, yet finding unrelated compatible donors continues to be difficult. Therefore, the European Union aims to facilitate patients in getting a secure,

efficient and egalitarian access to HSCT from unrelated compatible donors.

POSEIDON stands for 'Promoting optimisation, safety, experience sharing and quality implementation for donation organisation and networking in unrelated haematopoietic stem cell transplantation in Europe'. POSEIDON was a project funded by the EU in the framework of the EU Public Health Programme (2003–2008). During 42 months, from June 2007 to November 2010, the Institut National de la Santé et de la Recherche Médicale (France) coordinated the project, which was supported by seven associated partners from different Member States (Hungary, Norway, France and Spain).

The project focused on improving the steps prior to donation for transplantation, namely the recruitment of donors, typing strategies (the assessment of HSC compatibility with the potential recipient), the organisation of donor registries and cord blood banks, and donor search.

There are three EU Directives<sup>(66)</sup> that provide a common legal framework for HSCT in the EU. POSEIDON also gathered data on these Directives across Member States. This data provided key information about the status of the implementation of the Directives in each country and the difficulties experienced in their transposition.

### Encouraging a more egalitarian access to unrelated haematopoietic stem cell transplantation in Europe

One of the aims of POSEIDON was to encourage an egalitarian access to unrelated HSCT throughout the European Union. For this

<sup>(65)</sup> American Cancer Society: [www.cancer.org/acs/groups/cid/documents/webcontent/003215-pdf.pdf](http://www.cancer.org/acs/groups/cid/documents/webcontent/003215-pdf.pdf)

<sup>(66)</sup> Directive 2004/23/EC, Directive 2006/17/EC and Directive 2006/86/EC.

reason, the project also focused on the situation of minorities and immigrant populations in Europe (legal issues, health problems, etc.), as these groups may be more prone to having a limited access to HSCT. The actions taken in the EU towards the representation of these minorities in HSC registries were also analysed.

According to POSEIDON, there were inequalities in access to HSCT among minorities. Minorities coming from countries with large numbers of donors registered had usually access to these sources for transplantation through international exchanges. However, an important problem of access to HSCT was detected in other

communities, such as those coming from Africa, with scarce HSC registries in their countries of origin.

POSEIDON identified the Internet as an under-exploited tool with broad possibilities to enhance HSC recruitment of minority donors. According to the project, there should be a much more intensive use of the Internet to capture the attention of potential donors from specific ethnic minority groups.

The POSEIDON consortium with the financial support of the European Union promoted a better, safer and wider national and European landscape for HSC exchanges and HSCT.



### Further information:

Project website

<http://ec.europa.eu/eahc/projects/database.html?prjno=2006210>

### Project team:

Institut National de la Santé et de la Recherche Médicale  
37, allée Jules Guesde  
31073 Toulouse  
FRANCE  
Tel. +33 561145959  
Fax +33 561145623

### Associated partners:

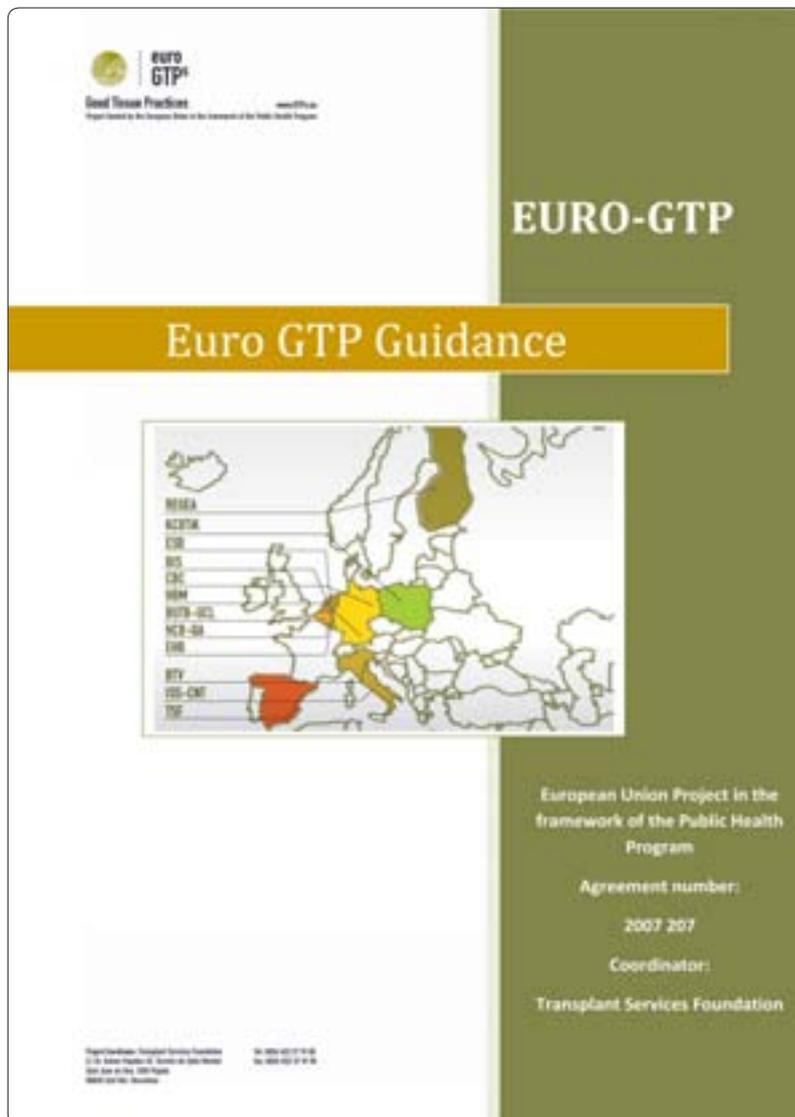
- Országos Gyógyintézeti Központ, Hungary
- Universitetet i Oslo , Norway
- Tundástársadalom Alapítvány, Hungary
- European Federation for Immunogenetics, France
- Universidad del País Vasco / Euskal Erriko Unibertsitatea , Spain
- Agence de la biomédecine , France
- Centre National de la Recherche Scientifique, France

### EU contribution

This project has received co-funding from the European Union in the framework of the **Public Health Programme 2003–2008** (Grant: 2006210).

## European Good Tissue Practices (Euro-GTPs)

*This project has received co-funding from the European Union in the framework of the **Public Health Programme 2003–2008** (Grant: 2007207).*



The Euro GTP Guidance document <sup>(67)</sup>

Euro-GTP stands for European Good Tissue Practices. It was a 3-year project funded by the European Union in the framework of the 2nd Health Programme. The project, which began in September 2008 and finished in October 2011, was coordinated by the Transplant Services Foundation (Barcelona, Spain), and involved 12 partners in total from seven different EU Member States (Netherlands, Italy, Germany, Belgium, Poland, Finland and Spain).

In Europe, there are regulations which provide the general basis for performing tissue banking activities in a professional and coherent manner<sup>(68)</sup><sup>(69)</sup><sup>(70)</sup>. However, it is important that the concrete procedures performed in tissue banking are harmonised among all tissue establishments in Europe so that high quality and the safety of transplanted tissues can be guaranteed.

### The objectives of the Euro-GTP project were:

- to develop detailed European good tissue practices for the activities carried out in tissue establishments<sup>(71)</sup>, in order to contribute to the harmonisation of these activities among European tissue establishments; to achieve this objective, the European Good Tissue Practice Guidance for tissue establishments activities was elaborated<sup>(72)</sup>;
- to develop a training model for tissue establishment personnel based on these good tissue practices.

According to the final report of the project, 'the aim was to apply these practices European-wide to increase the know-how and the level of performance of tissue banking staff, and to harmonise the techniques used in order to provide tissues for transplant of high quality

<sup>(68)</sup> Directive 2004/23/EC — 'Setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells'.

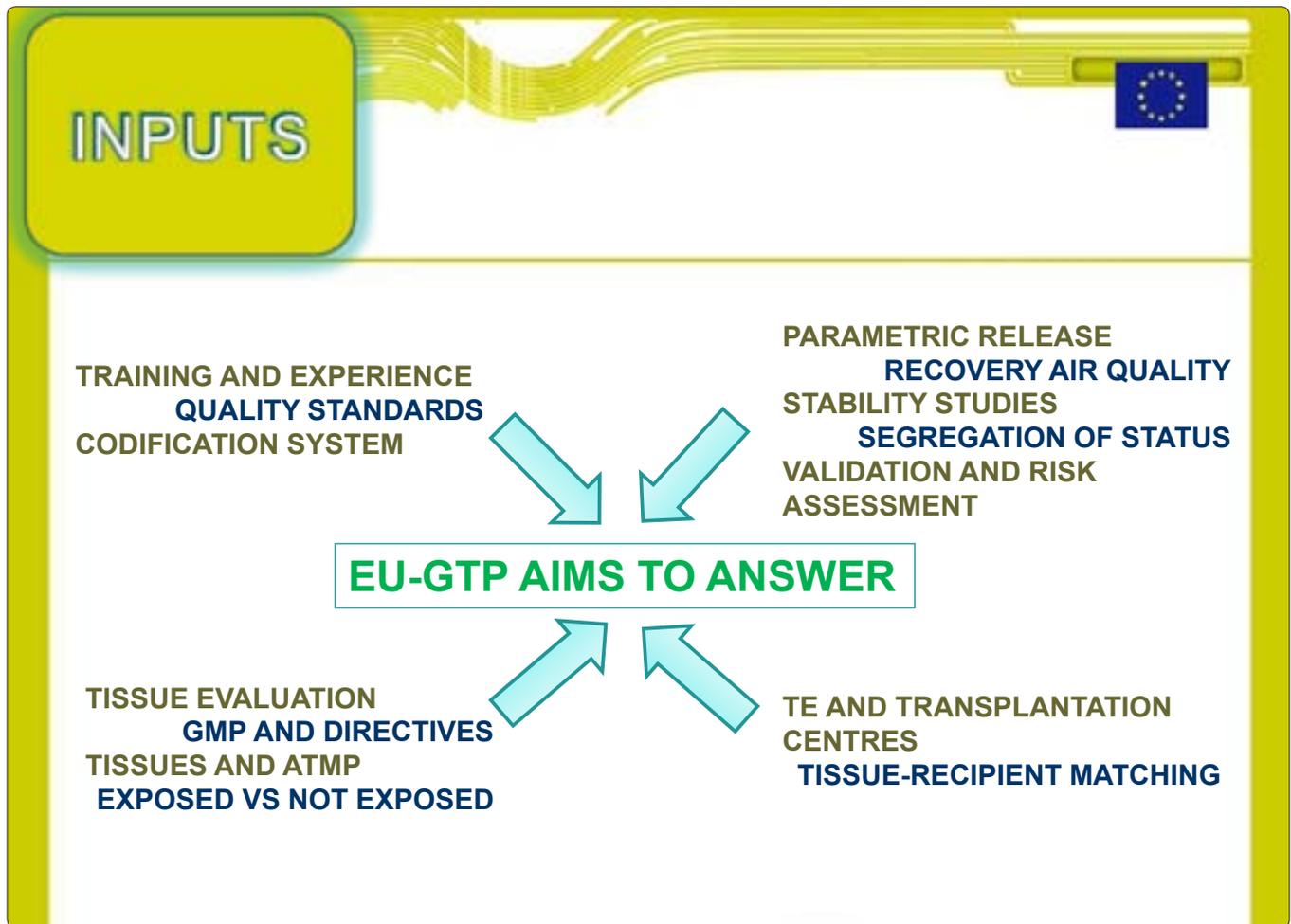
<sup>(69)</sup> Directive 2006/17/EC — 'Implementing Directive 2004/23/EC of the European Parliament and of the Council as regards certain technical requirements for the donation, procurement and testing of human tissues and cells'.

<sup>(70)</sup> Directive 2006/86/EC — 'Implementing Directive 2004/23/EC of the European Parliament and of the Council as regards traceability requirements, notification of serious adverse reactions and events and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cells'.

<sup>(71)</sup> A tissue establishment is a tissue bank or a unit of a hospital or another body where activities of processing, preservation, storage or distribution of human tissues and cells are undertaken. It may also be responsible for procurement or testing of tissues and cells.

<sup>(72)</sup> Euro-GTP Project. Euro GTP Guidance, <http://eurogtps.com/Portals/0/pdf/Euro%20GTP%20Final%20Delivery.pdf>

<sup>(67)</sup> <http://eurogtps.com/Portals/0/pdf/Euro%20GTP%20Final%20Delivery.pdf>



and safety, hence reducing the risk of disease transmission to recipients’<sup>(73)</sup>. Jaime Tabera, from the Transplant Services Foundation (Barcelona) and a member of the Euro-GTP team, stated that ‘Euro-GTP aims to provide guidance in areas where it is lacking or where the Directives are difficult to interpret, such as the cases that have emerged during the EUSTITE project’<sup>(74)</sup>.

Before starting the elaboration of the guidelines, the project team attempted to have a better understanding of the situation on regulations and tissue banking procedures. In order to do so, a number of activities were done: a questionnaire on the methods used for tissue banking processes was distributed to tissue establishments; a survey circulated among current and future European Union inspectors of tissue establishments with questions focusing on their audit findings, the difficulties they experienced in implementing the current regulation and their opinion about the

worth of a more detailed and realistic guidance at European level. Finally, relevant documents and regulations were analysed. As a result, the project team was able to define the contents of the European Good Tissue Practice Guidance.

### 1. The European Good Tissue Practice Guidance<sup>(72)</sup>

The European Good Tissue Practice Guidance provides a detailed information package for tissue bankers and tissue establishment inspectors in Europe. According to the project team, these guidelines describe the current minimum regulatory requirements of the European tissue and cells Directives <sup>(68)</sup><sup>(69)</sup><sup>(70)</sup> and go one step further by providing a set of practical recommendations for good practice in the European tissue establishments<sup>(72)</sup>. As stated by the authors, ‘the guidelines were developed to be a helpful tool for all kinds of tissue establishments in different phases of their development and evolution as well as for competent authorities when performing tissue establishments’ inspections’<sup>(72)</sup>.

<sup>(73)</sup> Euro-GTP Project, Final technical report.

<sup>(74)</sup> Eustite project, Deliverable 13, Final conference report.

As highlighted by the project team, this guidance drew upon the work of previously European Union funded projects, particularly the EQSTB project and the EUSTITE project. EQSTB published a Guide of Recommendations for Tissue Banking defining the fundamental quality and safety key points, a training system for tissue establishment personnel, a prototype of a tissue registry, and a model for auditing tissue establishments (Guide for Auditing). At the same time, EUSTITE developed guidance and training for Competent Authority inspectors along with tools and guidance for vigilance and surveillance. This demonstrates the strong and continuing commitment of the European Union in its concern to support harmonisation of activities among tissue establishments in Europe<sup>(72)</sup>.

The European Good Tissue Practice Guidance encompassed procedural recommendations on: (i) donor screening and selection for each tissue type; (ii) tissue procurement, processing, preservation and storage; and (iii) how to validate these processes. The guidance was structured in two main parts: 'generic good tissue practices' and 'tissue-specific good tissue practices'.

The generic section comprises practical instructions on: (i) generic processes carried out in tissue establishments, (ii) risk assessment, and (iii) validation methods for donor screening and tissue procurement, processing, preservation and storage, as well as basic requirements concerning infrastructure, personnel, documentation management, etc.

The tissue-specific sections comprise practical instructions on donor screening and tissue procurement, processing, preservation, storage and transportation related to skin, ocular, cardiovascular, musculoskeletal and amniotic membrane tissues.

The European Good Tissue Practice Guidance is available on the project website<sup>(75)</sup>.

## 2. Good Tissue Practice 'Hot Topics'<sup>(76)</sup>

The key issues and the issues not covered or partly covered by standards or regulation were identified and highlighted as 'Hot Topics' and

put together in a document. This document covers the following topics: donor selection; recovery and processing environments; tissue specific quality criteria; risk management; traceability and vigilance; validation; facilities disinfection; critical third-party agreements; import and export; continuity plans; and a tissue establishment dossier.

According to the project team, these Hot Topics are under regular revision. The document can be downloaded from the project website<sup>(77)</sup>.

## 3. Training model for tissue establishments personnel

Another main objective of the project was to develop a training model for staff of tissue establishments based on the defined good practices. As stated in the final report of the project, it was decided not to hold a residential training course given that the course was supposed to be based on the contents of the European Good Tissue Practice Guidance, which was in draft at that moment. For this reason, the residential training session was not organised during the period of the project<sup>(73)</sup><sup>(78)</sup>.

However, the Internet tool developed for the guidance and the Hot Topics was enhanced with a self-assessment instrument to allow professionals to verify their understanding and knowledge of good tissue practices. This training exercise is available in electronic form on the project website<sup>(79)</sup>. It can also be downloaded as a PDF file<sup>(80)</sup>. The project partners considered the learning needs in relation to the good practices developed in the project, and designed quiz questions aimed at highlighting those issues that were most important or most novel in their environment. According to the team, *'the tool allows many more professionals than would be able to attend a residential course to verify their understanding and knowledge of good tissue practices'*<sup>(73)</sup>.

<sup>(75)</sup> <http://eurogtps.com/PROJECTOUTCOMES/GUIDANCE/Tableof-Contents/tabid/143/Default.aspx>

<sup>(76)</sup> Euro-GTP Project, Euro GTP Hot Topics, <http://eurogtps.com/PROJECTOUTCOMES/EuroGTPHOTTOPICS/CONTENTS/tabid/221/Default.aspx>

<sup>(77)</sup> [http://eurogtps.com/Portals/0/pdf/GTP %20hot %20Topics.pdf](http://eurogtps.com/Portals/0/pdf/GTP%20hot%20Topics.pdf)

<sup>(78)</sup> Euro-GTP Project, Deliverable 9, Evaluation report.

<sup>(79)</sup> <http://eurogtps.com/PROJECTOUTCOMES/FinaltrainingmodelquestionnaireGtp/tabid/305/Default.aspx>

<sup>(80)</sup> <http://eurogtps.com/Portals/0/pdf/Final%20training%20model%20questionnaire.pdf>

**The Euro-GTP project contributed to a higher confidence in the exchange of tissues for transplant among the Member States**

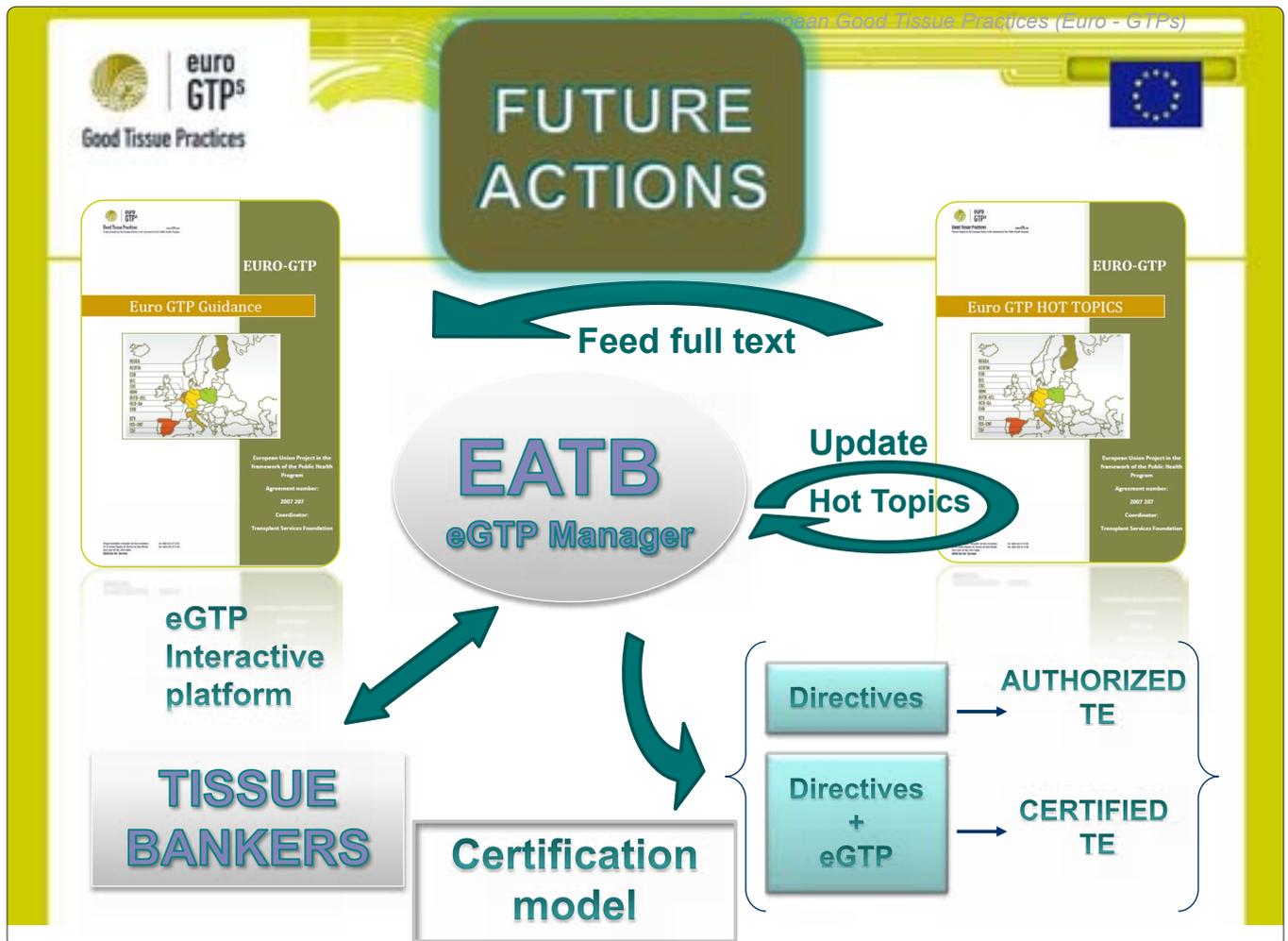
The Euro-GTP project provided specific practices to be followed in European tissue establishments in order to harmonise these decisive procedures in Europe. According to this project, apart from sharing a common regulation in the European Union, it is important that the concrete procedures performed in tissue banking are harmonised so that high quality and the safety of transplanted tissues can be guaranteed.

In this sense, the Euro-GTP project contributed to a higher confidence in the exchange of tissues for transplant among the Member States by bringing added value into the current EU legislation on tissue and cells.

All the guidelines generated during the project are available on the project website, mainly Guidance<sup>(72)</sup>, Hot Topics<sup>(76)</sup> and Training Exercise<sup>(80)</sup>. For more information, please visit the project website.



Webpage containing the guidance document (<http://eurogtps.com/>)





### Further information:

Project website

<http://ec.europa.eu/eahc/projects/database.html?prjno=2007207>

<http://eurogtps.com/>

Project team:

Transplant Services Foundation — TSF  
 c/ Mejia Lequerica, 1 — Edifici Helios 3  
 PO-BOX  
 08028 Barcelona  
 SPAIN  
 Tel. +34 932279190  
 Fax +34 932278188

### Associated partners:

- Charite-Universitätsmedizin Berlin — CBC, Germany
- Bio Implant Services Foundation — BIS Foundation, Netherlands
- Istituto Superiore di Sanita — ISS, Italy
- Banque Universitaire de Tissus — BUTB-UCL, Belgium
- Hornhautbank Muenchen Gemeinnutzige GmbH — UBM, Germany
- National Centre of Tissue and Cell Banking — NCTCB, Poland
- Hopital Central de la Base Reine Astrid — HCB-QA, Belgium
- Tampereen Yliopisto (University of Tampere) — REGEA, Finland
- Azienda Unita Locale Socio Sanitaria N°9 — U.L.S.S N°9, Italy
- European Homograft Bank — EHB, Belgium
- Stichting Euro Skin Bank — Huidbank — ESB, Netherlands

### EU contribution

This project has received co-funding from the European Union in the framework of the **Public Health Programme 2003–2008** (Grant: 2007207).

# Vigilance and Surveillance of Substances of Human Origin (SoHO V&S)

*This project has received co-funding from the European Union in the framework of the Health Programme 2008–2013 (Grant: 20091110).*

SoHO V&S is a 3-year project funded by the EU Second Programme of Community Action in the Field of Health. SoHO V&S stands for Vigilance and surveillance of substances of human origin. The project was launched in March 2010 and finished in February 2013. Coordinated by the Italian National Transplant Centre (Rome), the initiative has brought together nine partners from seven Member States. The World Health Organisation (WHO) and other collaborating partners from outside the European Union were also involved, which ensured that the guidance produced in this project reflects international needs and realities in the context of human tissues and cells for human application.

The SoHO V&S project aims to support EU Member States in the establishment of vigilance and surveillance systems for tissues and cells in transplantation and assisted reproduction. Vigilance and surveillance systems include ongoing data collection, analysis to convert this data into statistics, interpretation of this analysis to produce information and dissemination of this information to those who can take appropriate action<sup>(81)</sup>.

## Each Member State must put in place systems for vigilance of risks associated with tissues and cells in transplantation and assisted reproduction

More and more patients in Europe are treated with cells or tissues from a different country. Such transplants include bone marrow, cord blood or corneas, amongst others. Gametes and embryos also circulate for use in fertility treatments.

For this reason, tissues and cells for human application represent a key area where the European Union has introduced legislation to protect public health. Several EU

Directives<sup>(82)</sup><sup>(83)</sup><sup>(84)</sup> require each Member State to nominate Competent Authorities responsible for implementing regulatory activities in the field of human tissues and cells for transplantation and assisted reproduction. Moreover, each Member State must put in place systems for vigilance and surveillance of serious adverse reactions and serious adverse events associated with such a type of activities.

SoHO V&S is not the first EU-funded project addressing vigilance and surveillance in substances of human origin in the European Union, as it builds on the work done by the EUSTITE Project (2006–2009)<sup>(85)</sup>. EUSTITE identified the need for common guidelines on the reporting and investigation of adverse outcomes associated with collection, processing, storage, packaging and distribution of tissues and cells for human use. Therefore, SoHO V&S decided to work on this issue.

*“Tissues and cells for human application represent one of the key areas where the EU has introduced legislation to protect public health. It requires Member States to establish systems for reporting of serious adverse reactions and events and for forwarding annual reports of this activity to the European Commission.”<sup>(86)</sup>*

<sup>(82)</sup> Directive 2004/23/EC — ‘Setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells’.

<sup>(83)</sup> Directive 2006/17/EC — ‘Implementing Directive 2004/23/EC of the European Parliament and of the Council as regards certain technical requirements for the donation, procurement and testing of human tissues and cells’.

<sup>(84)</sup> Directive 2006/86/EC — ‘Implementing Directive 2004/23/EC of the European Parliament and of the Council as regards traceability requirements, notification of serious adverse reactions and events and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cells’.

<sup>(85)</sup> EUSTITE: European Union Standards and Training for the Inspection of Tissue Establishments.

<sup>(86)</sup> [http://ec.europa.eu/health/programme/docs/success\\_stories\\_hp\\_2008-2013\\_en.pdf](http://ec.europa.eu/health/programme/docs/success_stories_hp_2008-2013_en.pdf)

<sup>(81)</sup> [http://ecdc.europa.eu/en/healthtopics/spotlight/spotlight\\_surveillance/Pages/Key\\_message\\_1.aspx](http://ecdc.europa.eu/en/healthtopics/spotlight/spotlight_surveillance/Pages/Key_message_1.aspx)

For its aim to establish vigilance and surveillance systems for tissues and cells in transplantation and assisted reproduction, the project will introduce standard practices on how serious adverse events and serious adverse reactions associated with human tissue and cells are reported, evaluated and investigated. The emphasis will be put on investigation approaches, on the role of the clinical user, and on areas that need specific guidance, such as assisted reproduction and situations where illegal or fraudulent activities are suspected.

### Big steps have been taken so far to meet the project objectives

According to SoHO V&S, *'vigilance systems for tissues and cells in the European Union are generally at an early stage of development. There is a need for guidance and training of Competent Authority personnel, particularly in investigation'*<sup>(87)</sup>.

SoHO V&S is harmonising terminology and documentation, allowing for a consensus on how to exchange information among Member States. The guidelines produced will support the implementation of the regulation on the exchange of human tissues and cells, as well as the better control against illegal and fraudulent activities with these products.

The Spanish National Transplant Organisation (ONT), one of the project partners, conducted a survey in 2010 about the vigilance and surveillance systems for tissues and cells used in transplantation and in assisted reproduction in Europe<sup>(88)</sup>. All those responding to the survey questions indicated that they had a vigilance system in place in their country. The number of Member States with systems in place had increased from 15 (56 %) in 2009 to 23 (96 %) in 2010. Sixty-eight per cent of the respondents reported that they had national systems for issuing alerts when immediate action was required.

Furthermore, the survey indicated a high level of involvement of the Competent Authorities in the investigation of serious adverse events and reactions. On the other hand, according to the survey, there was a high interest in setting up an international investigation team available to all Member States for conducting particularly challenging



Project brochure <sup>(89)</sup>

investigations regarding serious adverse events and reactions. It is foreseen to publish the full survey report on the project website.

### Specific guidance for vigilance in assisted reproduction has been developed

The Agency of Biomedicine in France (an associated partner of the project) leads the task of exploring the specificities of vigilance and surveillance in assisted reproduction. After an international workshop and a series of drafting meetings, the vigilance tools developed by the EUSTITE project were adapted to the assisted reproduction context. Moreover, specific guidance to vigilance in this field has been produced and is available on the project website<sup>(90)</sup>.

<sup>(87)</sup> [www.sohovs.org](http://www.sohovs.org)

<sup>(88)</sup> [www.organsandtissues.net/index.php?id=91&tx\\_ttnews\[tt\\_news\]=574&cHash=08c5f51e0fa89fef161d5e403844e55e](http://www.organsandtissues.net/index.php?id=91&tx_ttnews[tt_news]=574&cHash=08c5f51e0fa89fef161d5e403844e55e)

<sup>(89)</sup> <http://www.sohovs.org/soho/>

<sup>(90)</sup> [www.sohovs.org/soho/file.php/1/Deliverable\\_5\\_WP5\\_ART\\_Vigilance.pdf](http://www.sohovs.org/soho/file.php/1/Deliverable_5_WP5_ART_Vigilance.pdf)

Many EU Competent Authorities for tissues and cells lack experience and training to investigate cases where illegal or fraudulent activity is suspected. The French Agency for the Safety of Health Products (AFSSAPS) leads a work package of the project, which aims to understand better the legal and regulatory framework in each Member State in relation to illegal and fraudulent activity in transplantation or assisted reproduction, and to produce specific guidance on this field.

To this end, a survey has been performed on the current approaches to detect and prevent illegal or fraudulent activity, gathering information from Member States on cases that have been investigated and concluded. Moreover, guidance to support Competent Authorities on the detection and management of illegal and fraudulent activity in the field of transplantation or assisted reproduction has been completed. According to the project team, the guidance developed is the first of its kind in the field of transplantation or assisted reproduction.

Prior to SoHO V&S, the EUSTITE project had identified the need for common guidelines on the investigation of serious adverse reactions and serious adverse events in the field of substances of human origin. SoHO V&S has taken over this task and is now working actively on it. According to Dr Alessandro Nanni Costa, the SoHO V&S project coordinator, the consortium has developed the draft of the 'Guidance for EU tissue and cell Competent Authorities on communication and investigation of serious adverse events and reactions associated with human tissues and cells'. This draft was developed taking into account the outputs of international events in the field, particularly the ones resulting from the NOTIFY meeting held jointly with the WHO in Bologna (Italy) in February 2011<sup>(91)</sup>. Moreover, the draft has been the subject of three focus group consultations: one in the United Kingdom, one in Germany and another in Spain during February 2012. According to the project leader, this guidance has been submitted to wider consultation before the final version is released.

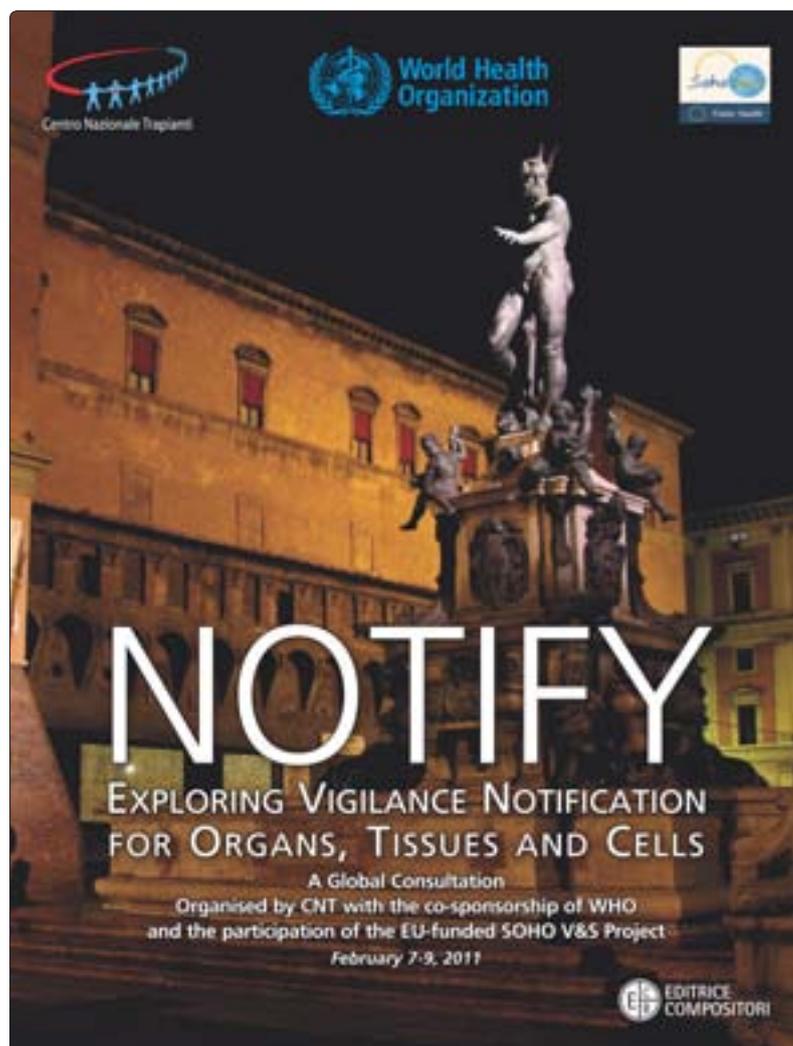
The Polish partner of the project (Krajowe Centrum Bankowania Tkanek i Komorek) supported by the major professional societies in the field, is developing guidance for clinicians that use tissues and cells for assisted reproduction or transplantation. According to the project team, this guidance recognises the critical role of clinicians in the vigilance and surveillance of tissues and cells. The text will address the responsibilities of

clinicians in relation to traceability and appropriate storage and use as well as their role in the identification, reporting and investigation of adverse reactions in their patients. The guidance is to be published as a booklet and made available to EU Competent Authorities for translation and distribution nationally as they wish<sup>(92)</sup>.

According to the project coordinator, training courses have been designed for individuals who are actively involved in vigilance of tissues and cells. These courses constitute a unique

“Citizens can be reassured that tissue and cell transplants are safer in the EU due to this widening knowledge, harmonisation and better connectivity between Member States.”

Deirdre Fehily, SoHO V&S project



Report: *Promoting Vigilance and Surveillance of Organs, Tissues and Cells* <sup>(93)</sup>

<sup>(91)</sup> [www.sohovs.org/soho/file.php/1/Final\\_Programme\\_NOTIFY.pdf](http://www.sohovs.org/soho/file.php/1/Final_Programme_NOTIFY.pdf)

<sup>(92)</sup> [www.sohovs.org/soho/mod/resource/view.php?id=39](http://www.sohovs.org/soho/mod/resource/view.php?id=39)

<sup>(93)</sup> <http://www.notifylibrary.org>

opportunity for vigilance professionals to work together with colleagues from other Member States<sup>(88)</sup>. Each course consists of a four week e-learning module followed by a 2-day residential course. The first course, which was held in Ireland and finished with the 2-day residential course (18–20 June 2012), was very highly evaluated by the participants, according to the project coordinator.

A new area dedicated to the SoHO V&S project has been created in the Eurocet website (European Registry for Organs, Tissues and Cells)<sup>(94)</sup>, in order to support the sharing of information between Competent Authorities in

the European Union as they develop their vigilance and surveillance systems.

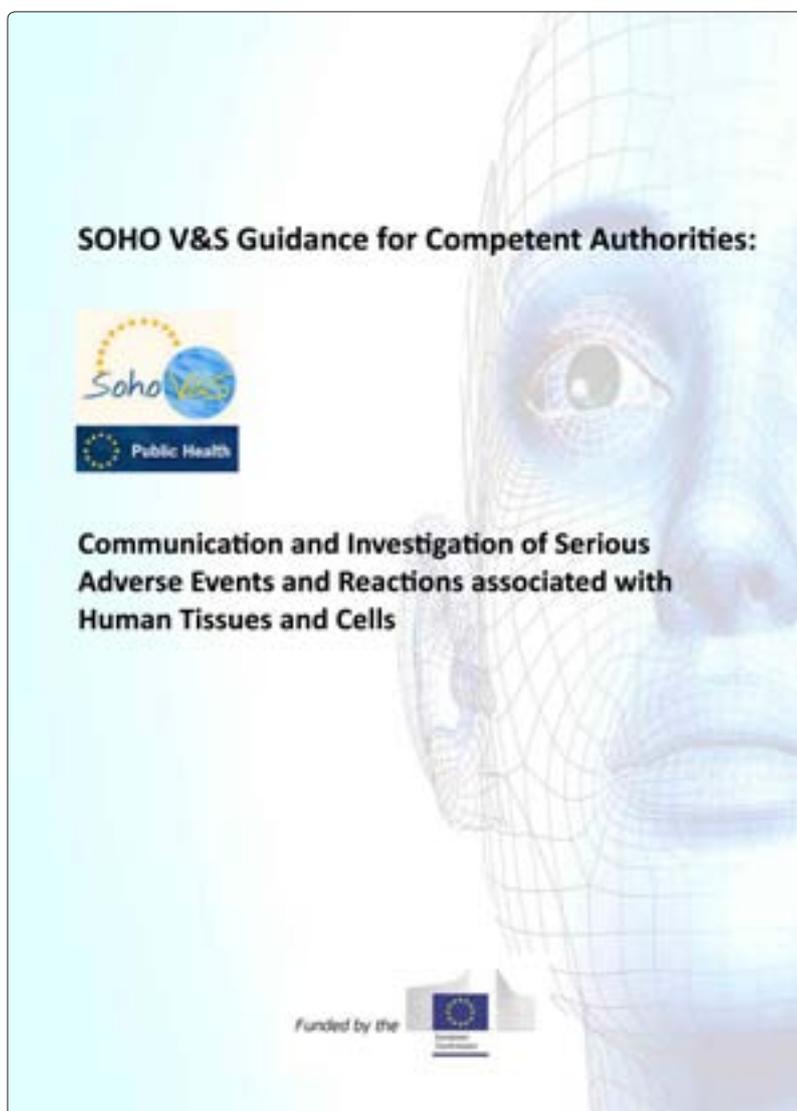
### Bologna Initiative for Global Vigilance and Surveillance (BIG V&S)

From September 2010 to February 2011, the WHO, the Italian National Transplant Centre and the SoHO V&S project joined forces to launch the NOTIFY project. NOTIFY culminated in a large international workshop that was held in Bologna (Italy) in February 2011 with the participation of over 100 invited experts from 36 countries.

During the workshop, the Bologna Initiative for Global Vigilance and Surveillance (BIG V&S) was established and a number of outcomes were agreed, such as the creation of a new dedicated website for the dissemination of information regarding adverse events and reactions for organs, tissues and cells (Notify Library)<sup>(95)</sup>.

The Human Tissue Authority (United Kingdom) will organise the global vigilance and surveillance conference in the United Kingdom that will last a day and half and was held in February 2013.

The SoHO V&S project was selected as one of the 20 successful projects funded by the EU Health Programmes since 2003<sup>(96)</sup>. SoHO V&S shows how the Health Programme has helped to raise awareness on the role of vigilance and surveillance as a fundamental instrument for improving safety in tissue and cell transplantation and assisted reproduction.



*The published guidelines on 'V&S in Assisted Reproduction Technologies', 'Communication and Investigation of Adverse Reactions and Events', 'The Detection and Investigation of Suspected Illegal or Fraudulent Activity', 'V&S in Living Donors', 'V&S Guidance for Clinical Users' (available at: <http://www.sohovs.org/soho/>)*

<sup>(94)</sup> <http://registry.eurocet.org/soho/>

<sup>(95)</sup> [www.notifylibrary.org](http://www.notifylibrary.org)

<sup>(96)</sup> [http://ec.europa.eu/health/programme/docs/success\\_stories\\_hp\\_2008-2013\\_en.pdf](http://ec.europa.eu/health/programme/docs/success_stories_hp_2008-2013_en.pdf)



### Further information:

Project website

<http://ec.europa.eu/eahc/projects/database.html?prjno=20091110>

<http://www.sohovs.org/soho/>

### Project team:

Istituto Superiore di Sanità — ISS

Viale Regina Elena 299

PO-BOX

00161 Rome RM

ITALY

Tel. +39 0649904040

Fax +39 0649904101

### Associated partners:

- Agence de la Biomedecine, France
- Agence Française de Sécurité Sanitaire des Produits de Santé, France
- Donor Action Foundation, Belgium
- Human Tissue Authority, United Kingdom
- Irish Medicines Board, Ireland
- Krajowe Centrum Bankowania Tkanek i Komorek, Poland
- Organización Nacional de Trasplantes, Spain
- The Human Fertilisation and Embryology Authority, United Kingdom

### EU contribution

This project has received co-funding from the European Union in the framework of the **Health Programme 2008–2013** (Grant: 20091110).

## European Quality System for Tissue Banking Project (EQSTB)

*This project has received co-funding from the European Union in the framework of the Public Health Programme 2003–2008 (Grant: 2003209).*

Tissues and cells donated altruistically can save and improve the lives of recipients. For this reason, the transplantation of human tissues and cells is a strongly expanding field of medicine offering great opportunities for the treatment of still incurable diseases. The quality and safety of these substances should be ensured, particularly in order to prevent the transmission of infectious diseases<sup>(97)(98)(99)</sup>.

### Tissue banking activity background is very diverse in Europe

A tissue establishment is a tissue bank or a unit of a hospital or another body where activities of processing, preservation, storage or distribution of human tissues and cells are undertaken. It may also be responsible for procurement or testing of tissues and cells<sup>(97)</sup>.

The origin and the organisation of the tissue establishments in Europe are greatly unlike. Security and safety may vary depending on the tissue bank that has the control over the whole process, from donor selection criteria to tissue suitability for its transplantation. The European Quality System for Tissue Banking (EQSTB) project emerged as a result of this situation.

The EQSTB project was funded by the European Union, specifically by DG SANCO and it was coordinated by Hospital Clinic (Barcelona, Spain). From May 2004 until May 2007 it involved 15 partners (representing different national organisations and tissue establishments) from 12 European countries.

The project's main goal was to analyse the factors that may influence the final tissue quality and

safety for its transplantation. Further, the project aimed to develop the method to ensure the standards of quality and safety in relation to tissue banking activities demanded by Directive 2004/23/EC<sup>(97)</sup>. To achieve these objectives, the tasks in the project were divided into four working groups:

1. The **Standards Working Group** performed an analysis of the different standards that were followed in the participating countries. This allowed creating *The Guide of Recommendations for Tissue Banking*<sup>(100)</sup>, which included the following contents:

- a description of the different quality systems that apply to tissue banking and a provision of the general quality system requirements;
- the legal and regulatory framework regarding tissue banking activities in Europe;
- a description of the different standards on tissue banking activities that are available in Europe;
- a description of the quality and safety key points that are considered fundamental in tissue banking.

According to Dr Martí Manyalich (Hospital Clinic, Barcelona), the project coordinator: '*The Guide of Recommendations for Tissue Banking was distributed across centres and since then is considered as a reference manual in Europe. These Guides are being used in the routine of a number of tissue establishments around the world. We can mention among these countries Brazil, Colombia and Lebanon.*'

This Working Group also surveyed tissue establishments to diagnose their capability to fulfil the European legislation on tissues and cells. The survey showed that most partner countries had more or less already implemented the EU Directives, or were in the process of adopting them<sup>(101)</sup>.

<sup>(97)</sup> Directive 2004/23/EC — 'Setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells'.

<sup>(98)</sup> Directive 2006/17/EC — 'Implementing Directive 2004/23/EC of the European Parliament and of the Council as regards certain technical requirements for the donation, procurement and testing of human tissues and cells'.

<sup>(99)</sup> Directive 2006/86/EC — 'Implementing Directive 2004/23/EC of the European Parliament and of the Council as regards traceability requirements, notification of serious adverse reactions and events and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cells'.

<sup>(100)</sup> Guide of recommendations for tissue banking. EQSTB (DG Sanco Project — European Commission). First edition: September 2007.

<sup>(101)</sup> European Quality System for Tissue Banking Project, Final Report 2004–2007 Period, Agreement Number 2003209, [http://ec.europa.eu/health/ph\\_projects/2003/action2/docs/2003\\_2\\_06\\_frep.pdf](http://ec.europa.eu/health/ph_projects/2003/action2/docs/2003_2_06_frep.pdf)

### The prototype of the registry proves that it would be possible to exchange tissues between establishments across Europe with such a database

2. The **Registry Working Group** created a prototype of an online European multinational musculoskeletal tissue registry for the entire banking process, including donation, processing, preservation, traceability, clinical application and adverse reactions after transplantation.

A database and a web application were developed, and a search engine function was created and put at the disposal of the participating tissue establishments. During the last year of the project, four partners performed a pilot data charge to validate the database. Each of them introduced 350 musculoskeletal tissue products into the registry, making a total of 1 400 inserted grafts. The validation test concluded with positive feedback from the partners involved in the data charge<sup>(101)</sup>.

A small document with the general indications for the development and management of a computerised registry for tissue establishments was provided to the European Commission, with strong emphasis on data traceability and data protection. According to the project team: *'The prototype of the registry proved that it would be possible to exchange tissues between establishments across Europe with such a database. It was challenging to harmonise the tissue product list, and, for this reason, it would be interesting to have in the future a common coding system for all tissue establishments in Europe'*<sup>(101)</sup>.

As Dr Martí Manyalich said, *'the first version of the registry was developed during the project timeline and has been improved and adapted continuously in order to satisfy each centre needs. This served as a starting point and model for the other registries that are being created afterwards.'*

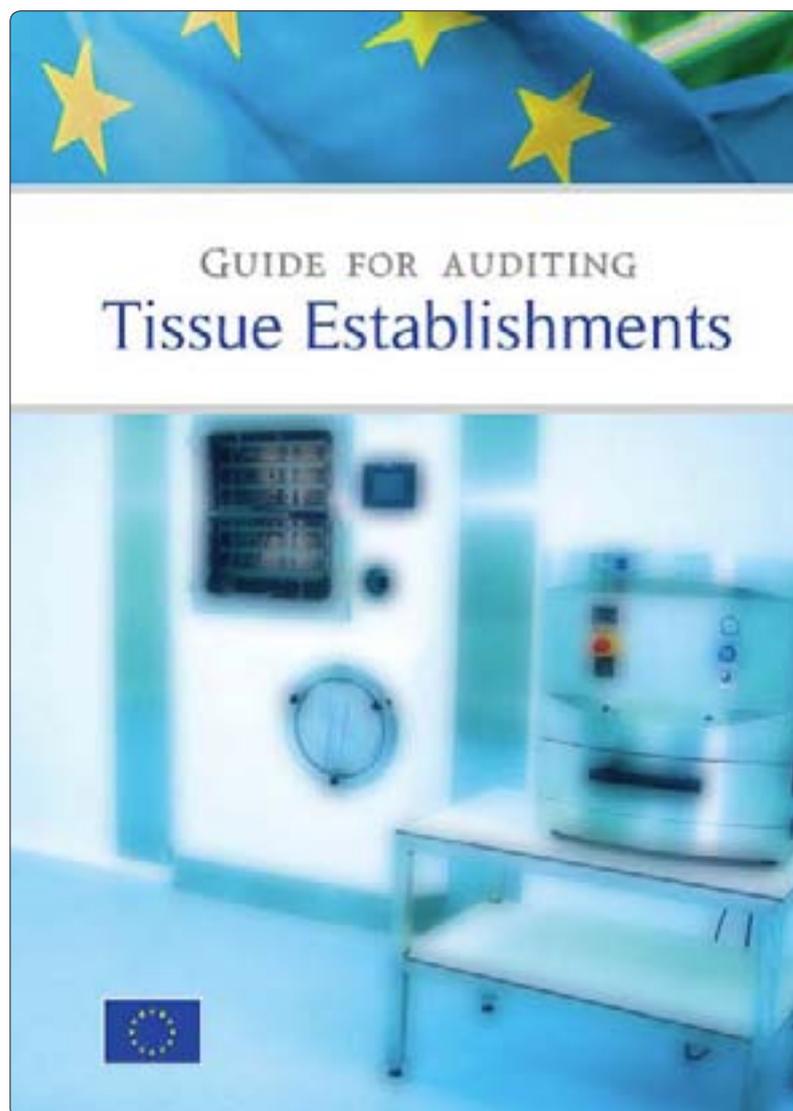
### A specialised training model for tissue bank personnel was designed and validated

3. The **Training Working Group** identified training needs for tissue bank personnel that could afterwards become a method of qualifying personnel and the approved training model adopted in the European Union. It was decided

that the training model should be structured into two complementary courses: an online course of approximately 2 months and one face-to-face course of 2 days.

“*Most tissue establishments had more or less already implemented the European legislation about tissues and cells, or were in the process of adopting them.*”

A review of the existing tissue banking training courses in Europe identified the 'International Online Tissue Banking Course' from the University of Barcelona. This course seemed to fit extremely well with the aims of the project. As a result, it was adopted and its contents and structure were further improved. Regarding the face-to-face course, it was agreed that it should complement the online course and also cover practical aspects that this one could not.





According to the project coordinator, this course structure permits a major flexibility for participants and reduces travel and accommodation expenses. The online education modality involves the development of a flexible, interactive and bidirectional teaching and learning action. The face-to-face course reinforces the knowledge through experience and is designed to put into practice the knowledge acquired in the online modules.

A pilot training course was performed in the last year of the project. Twenty-eight tissue banking practitioners recruited on a voluntary basis from Belgium, Finland, France, Germany, Italy, Latvia, Poland, Portugal, Romania, Slovak Republic, Slovenia, Spain, the Netherlands and the United Kingdom performed both the online and the face-to-face courses. The participants, who were evaluated by answering questionnaires before and after they took the courses, improved their knowledge after receiving the training and all of them received the corresponding certification. The organisational aspects of the course as well as the content were assessed, and the average scores obtained were high. Further, the model could be improved with the students' suggestions<sup>(101)</sup>.

*'The training model suggested during the project is widely used so far, and a significant number of countries, not only European but around all over the world, are applying this training programme,'* confirmed the project coordinator.

**4. The Auditing Working Group** received the task to design a European Auditing Model of tissue establishments based, among other factors, on the EU Directives on tissues and cells. With this aim, the Guide for Auditing Tissue Establishment<sup>(102)</sup> was developed, which provided tissue banking experts with a tool to audit tissue establishments based on quality and safety key points and the EU Directives. There was a checklist provided with a set of questions that can be used as a self-assessment tool so that the tissue establishment can audit itself.

For a more detailed description of the European Quality System for Tissue Banking project and its outputs, please read the final report of the project<sup>(101)</sup>.

<sup>(102)</sup> Guide for Auditing Tissue Establishment. EQSTB (DG SANCO Project — European Commission). First edition: September 2007.

### Further information:

Project website

<http://ec.europa.eu/eahc/projects/database.html?prjno=2003209>

### Project team:

Hospital Clinic I Provincial De Barcelona

Villaroel, 170

PO-BOX

08036 Barcelona

SPAIN

Tel. +34 932275400

Fax +34 932275454

### Associated partners:

- Transplant Services Foundation, Spain
- Belgian University Tissue Bank, Belgium
- Agence de Biomédecine, France
- Deutsches Herzzentrum Berlin, Germany
- I.R.C.C.S. Istituti Ortopedici Rizzoli, Italy
- BIS Foundation, Netherlands
- Netherlands Bone Bank Foundation, Netherlands
- Centro Nazionale Trapianti, Italy
- Organización Nacional De Trasplantes, Spain
- Tampere University Tissue Bank, Finland
- North London Tissue Bank, United Kingdom
- Ruzinov General Hospital Bratislava, Slovakia
- State Forensic Medicine Centre, Latvia
- National Centre of Tissue and Cell Banking, Poland
- University of Medicine and Pharmacy 'Victor Babes', Romania

### EU contribution

This project has received co-funding from the European Union in the framework of the **Public Health Programme 2003–2008** (Grant: 2003209).

## Building reference compendia for the application of a single European coding system for tissues and cells (Eurocet128, EAHC/ 2011/HEALTH/03)

*This service contract is financed from the European Union in the framework of the Health Programme 2008–2013 (Contract EAHC/2011/HEALTH/03, 20116102).*

Eurocet128 is a service contract funded by the European Union within the EU Health Programme framework. The initiative, launched in December 2011 and with a 30-month duration until June 2014, was conceived by a consortium of two partners: the Italian National Transplant Centre (which leads the project) and Artman Technologies, a company based in Slovakia with experience in designing and implementing information technology systems for traceability and management of transplantation activities.

The International Council for Commonality in Blood Banking Automation (ICCBBA)<sup>(103)</sup> is also involved as a subcontractor in the Eurocet128 project. The ICCBBA is an international organisation which manages and develops the ISBT 128, which is the global standard for the identification, labelling and information processing of human blood, cell, tissue and organ products across international borders and different healthcare systems. According to the ICCBA, *'by featuring a unique, highly flexible, and comprehensive coding method for every collected product, ISBT 128 provides international consistency to support the transfer, transfusion, or transplantation of blood, cells, tissues and organs'*<sup>(104)</sup>.

### It is essential to maintain traceability of tissues and cells

Tissues and cells such as corneas, heart valves, cord blood or bone marrow are used in transplant procedures to repair or replace damaged tissues or cells. Moreover, fertility treatments frequently involve the manipulation and transfer of gametes (sperm or eggs) or embryos. In these activities, it is essential to maintain traceability, which means that the tissues or cells can always be linked back to the original centre where they were collected, as well as to their original human origin<sup>(105)</sup>.

According to Directive 2004/23/EC<sup>(106)</sup> on tissues and cells, Member States shall establish a system for the identification of all human tissues and cells procured, processed, stored or distributed on their territory, in order to ensure their traceability from the donor to the recipient and vice versa. This Directive also requires designing a single European coding system to provide information on the main characteristics and properties of tissues and cells.

### Eurocet128 seeks to implement a single coding system in the European Union

The primary aim of the Eurocet128 project is to support the traceability of human tissues and cells that are applied to patients in the European Union. To achieve this goal, Eurocet128 will develop and implement a single European Coding System, which will be allocated to all donated material at the tissue establishment. This system will allow human tissues and cells to be categorised in a reliable way for clinical use, for activity reporting or for vigilance and surveillance purposes. Furthermore, it will allow

#### Donation identification

ISO country identifier	TE code	Unique donation number
Two characters (alphabetic)	Six characters (alpha/numeric)	13 characters (alpha/numeric)

#### Product identification

Coding system identifier	Product code	Split number	Expiry date
One character (alphabetic)	Seven characters (alpha/numeric)	Three characters (alpha/numeric)	Eight characters (numeric)

*The European Coding System proposed by Eurocet128*

<sup>(103)</sup> [www.iccbba.org](http://www.iccbba.org)

<sup>(104)</sup> [www.iccbba.org/home/isbt-128-basics/what-is-isbt-128](http://www.iccbba.org/home/isbt-128-basics/what-is-isbt-128)

<sup>(105)</sup> [www.eurocet128.eu](http://www.eurocet128.eu)

<sup>(106)</sup> Directive 2004/23/EC — 'Setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells'.

to link back to the original centre where cells and tissues were collected, as well as to their original human origin by improving traceability of these substances across the EU.

**By using the same European coding system, each donated material will be allocated a single code at the tissue establishment**

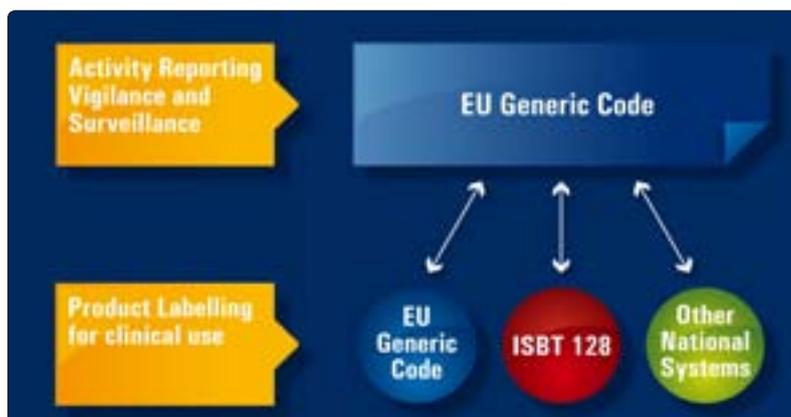
The work of the consortium is divided into several activities.

**1. Provide, test and find consent among Member States for a compendium of tissue establishments in the EU, as well as their respective codes**

Tissue establishments are centres that receive, test, process, store and distribute tissues or cells (including gametes and embryos) for human application. Eurocet128 aims to develop a tissue establishment compendium in order to provide a publicly accessible list of authorised tissue establishments in the European Union with their relevant identifying codes and a specific minimum set of information.

Eurocet128 is not the first EU-funded project addressing the traceability of human tissues and cells applied to patients in the European Union as the Tissue Establishment Compendium will be constructed on the work previously done by EURO CET<sup>(107)</sup> (European network of the competent authorities for tissues and cells). This was also an EU-funded project, although in this case under the e-TEN (trans-European e-services) programme, which contributed to make e-services available throughout the European Union<sup>(108)</sup>. Today the EURO CET network collects from EU Competent Authorities information on tissue establishments, and on activities in relation to tissues, haematopoietic and reproductive cells donation and transplantation (to learn more about the EURO CET network, please visit its website: [www.eurocet.org](http://www.eurocet.org)).

The Eurocet128 consortium intends to develop a procedure for a continuous updating of the tissue establishments list with details on the specific tissues and cells types managed, as well on specific activities authorised. The codes



*Eurocet128 will attempt to ensure that the European Coding System is compatible with the existing national systems and international initiatives to achieve global harmonisation on terminology and coding.*

for the tissue establishments will be allocated in line with the Single European Coding System.

*“By using the same European coding system, each donated material will be allocated a single code at the tissue establishment.”*

**2. Provide, test and find consent among Member States for a compendium of tissue and cells’ products and their respective alpha-numeric codes**

The Product Compendium will be a list of types of tissues and cells with agreed descriptions. Thus, for example, the tissue ‘cornea’, independently from the country of origin or the tissue establishment where it was processed, will always conform to the same European Product Code, which will correctly identify the product ‘cornea’. This will provide a means of harmonising product descriptions and coding throughout the European Union.

Eurocet128 will attempt to ensure that the European Coding System is compatible with the existing national systems and international initiatives to achieve global harmonisation on terminology and coding.

**3. Provide an online code-translator application to code/decode alphanumeric codes and textual information**

The Tissue Establishment Compendium and the Product Compendium will be implemented via the Code Translator, an online application. Tissues and cells professionals, clinical users and

<sup>(107)</sup> [www.eurocet.org](http://www.eurocet.org)

<sup>(108)</sup> [http://ec.europa.eu/information\\_society/activities/eten/index\\_en.htm](http://ec.europa.eu/information_society/activities/eten/index_en.htm)



Project leaflet (<http://www.eurocet128.eu>)

regulators will be able to enter the application for translating alphanumeric codes into textual information, as well as textual information into alpha-numeric codes. In particular, the application will convert tissue establishments and product codes from/into detailed text information, such as the names of the contact person, address, contact details, tissue type, expiry date of the products, etc. Therefore, as states the project team, *'the code translator will allow those who receive tissues or cells for human use to immediately establish both the origin and the description of the product'*<sup>(107)</sup>.

#### 4. Set up the code-translator application on the website of an EU agency, which will host, run, maintain and further develop the system by the end of the project

Eurocet128 plans to test in at least five EU Member States the use of both the compendia and the online code translator application in a pilot phase involving tissue establishments

and Competent Authorities. As stated by Eurocet128 in its project protocol, this pilot phase should involve diverse types of tissue establishments (e.g. bones, cord blood, bone marrow, skin, cornea, assisted reproduction facilities, etc.).

As soon as these tools are fully developed and tested, they will be available on the web together with guidance and manuals for users. Eurocet128 aims to provide a system that is user-friendly and compatible in terms of software and technology with the requirements of the corresponding hosting European Union agency, for example, with those of the European Medicines Agency.

Therapies based on tissue and cell trans-

plants are becoming ever more numerous and varied. The process — including tissue procurement, product manufacture and actual grafting — involves many complex and interrelated steps<sup>(109)</sup>. Eurocet128 will contribute to create a single European Coding system, which will ensure proper identification of the donor and rapid traceability of all donated tissues and cells. This system will be crucial to ensure the quality and safety of tissues and cells and to comply with the standards established in the European Union legislation.

For further information, please download the leaflet of the project<sup>(110)</sup>, which contains detailed information about this initiative, or visit the project website.

<sup>(109)</sup> [http://ec.europa.eu/health/blood\\_tissues\\_organ/tissues/index\\_en.htm](http://ec.europa.eu/health/blood_tissues_organ/tissues/index_en.htm)

<sup>(110)</sup> [www.eurocet128.eu/eurocet128.pdf](http://www.eurocet128.eu/eurocet128.pdf)

# EUROCET128

## Further information:

Project website  
<http://www.eurocet128.eu>

## Project team:

Istituto Superiore di Sanità — ISS  
National Italian Transplant Centre (CNT)  
Viale Regina Elena 299  
PO-BOX  
00161 Rome RM  
ITALY  
Tel. +39 0649904040  
Fax +39 0649904101

## Consortium partners:

- Artman Technologies, Bratislava, Slovakia (<http://www.artman.sk/>)
- The International Council for Commonality in Blood Banking Automation (ICCBBA) (<http://www.iccbba.org/>)

## EU contribution

This service contract is financed from the European Union in the framework of the **EU Health Programme 2008–2013** (Contract EAHC/2011/HEALTH/03, 20116102).

## Evaluation of legislation and related guidelines on the procurement, storage and transfer of human tissues and cells in the European Union — an evidence-based impact analysis (Tiss.EU)

*This project has received co-funding from the European Union in the framework of the 7<sup>th</sup> Framework Programme (Grant: 202204).*

Biobanks are organised collections where human tissues and cells are gathered, stored and classified, in order to distribute them among researchers for research projects. For example, samples of blood, skin, bone or tumours are collected. Biobanks range widely in scope from small disease specific collections to large-scale population-based repositories, and may be public or commercial<sup>(11)</sup>.

Cells and tissues collected in biobanks have gained great importance for biomedical research, as they can help to understand diseases and develop effective therapies. For this reason, the European Union actively encourages the networking of biobank initiatives.

### Biobank research depends on the availability of a large number of samples and the consolidation of collections across country borders

European Union legislation has dealt with the handling of human tissues and cells by regulating its clinical applications, but it does not cover its uses in the research field. Moreover, the regulation of the practices in biobanking research is heterogeneous across Member States, and a European Union regulation on biobanking for research is still missing. This can be a serious threat to transnational biomedical research involving human samples, by limiting access to samples and data. This is the context in which the Tiss.EU project was conceived.

Tiss.EU stands for Evaluation of legislation and related guidelines on the procurement, storage and transfer of human tissues and cells in the European Union — an evidence-based impact analysis. The project, funded by the European Union as a part of the Seventh Research Framework Programme, ran from April 2008 until March 2011, and was coordinated by the University of Goettingen, in cooperation with the University of Hannover, both of them located in Germany. It involved 10 partners (representing different universities and research institutions) from nine different Member States (Germany, United Kingdom, Sweden, Hungary, Italy, Ireland, France, Netherlands and Lithuania).

The Tiss.EU project analysed the ethical and legal regulation of human tissue and biobank research across the then 27 European Member States plus Switzerland, attempting to identify



*The Ethical and Legal Regulation of Human Tissue and Biobank Research in Europe* ([http://webdoc.sub.gwdg.de/univerlag/2011/tiss\\_eu\\_book.pdf](http://webdoc.sub.gwdg.de/univerlag/2011/tiss_eu_book.pdf))

<sup>(11)</sup> Cambon-Thomsen A, et al. Eur Respir J 2007; 30(2): 373–82.

regulation deficits and inconsistencies. The project focused on four aspects:

1. procurement, storage and transfer of tissue and cells for research;
2. rights and entitlements to tissue and cells;
3. anonymisation and pseudonymisation to protect privacy rights;
4. research using biobanks.

## I. Procurement, storage and transfer of tissue and cells for research purposes

Harmonisation in these aspects appears particularly difficult in the European Union, since regulations are divergent between Member States and may differ even at the level of institutions. According to Katharina Beier and Silvia Schnorrer, researchers of the project, *‘the United Kingdom, for example, has a discrete law and other reference acts on human tissue, whereas countries like Malta rely mainly on EU legislation’*<sup>(112)</sup>. In certain areas, such as consent procedures for the protection of tissue donor autonomy, standards varied dramatically. However, some common patterns were also identified. For example, in relation to the transfer of data and samples, the receiving institution or country usually adheres to the domestic rules of the sending country<sup>(118)</sup>.

## II. Rights and entitlements to tissue and cells — balancing the interests of donors, researchers and companies

Traditionally, the European provisions assert that *‘the human body and its parts shall not, as such, give rise to financial gain’*<sup>(113)</sup>, so in most Member States tissue donors have no proprietary rights in their biological materials and may not receive any remuneration from them. On the other hand, researchers or companies may derive profits from these tissues. In this context, the non-commercialisation principle

may no longer apply if human bodily materials turn into products (that is the case of Germany, for example)<sup>(114)</sup>.

The first international workshop within Tiss.EU about this focal theme of the project, that is, ‘Rights and entitlements in human tissue and cells’, was celebrated in Hannover. In summary, the contributions at the workshop reinforced the exigency to address the legal challenges of human tissue research thoroughly from an inter-European perspective. In particular, this workshop revealed fundamental questions of human tissue research that are only partly answered by national or EU law. However, according to the final conclusions of the workshop, the existing concordances in the national legal approaches on biobanking in Germany, Austria and Switzerland displayed a promising starting point for further legal adjustments within the field<sup>(118)</sup>.

## III. Anonymisation and pseudonymisation to protect privacy rights — the transfer of cells and tissues also concerns the right to privacy

The need for protection of privacy is widely acknowledged in the European Union. In most Member States, the protection of samples and data is regulated by national data protection laws based on the European Data Protection Directive<sup>(115)</sup>, which guarantees basic regulation across Member States.

The European Data Protection Directive makes several exemptions for the use of health data *‘for reasons of substantial public interest’*. What is contested, however, is whether these exemptions also apply to research; biobanks storage of human tissues transcends clinical purposes and is not aimed to treat an immediate health threat. According to the project team, *‘in cases as these, issues of consent and anonymisation rise to the fore’*<sup>(118)</sup>.

Personal and genetic data have a special importance in ethics and law because of their meaningfulness to personal qualities such as, for example, dispositions to diseases. For this reason, the information stored in biobanks

<sup>(112)</sup> Ethical and legal aspects of human tissue and biobank research in Europe: Report of the Tiss.EU project and its results, 2011.

<sup>(113)</sup> See, for example, the European Convention on Human Rights and Biomedicine (1997) or the Council of Europe’s Recommendation 2006(4) on research on biological materials of human origin.

<sup>(114)</sup> C Lenk. Berliner Debatte Initial 2010:21(4); 9–18.

<sup>(115)</sup> Directive 1995/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data (European Data Protection Directive).



The project website (<http://www.tisseu.uni-hannover.de>)

should not lead to identification of the donors and infringe their privacy rights. This is what institutions that manage biobanks aim to prevent by implementing the anonymisation and pseudonymisation of samples.

According to the project team, 'there is considerable disagreement about the provisions of anonymisation and pseudonymisation of samples and data across the Member States'<sup>(118)</sup>. Moreover, taken together, the contributions of the project workshops suggested that, although the anonymisation of samples and data might be the most effective means of protecting donors' privacy, 'in the context of human tissue and biobank research outright anonymisation might neither be desirable, nor obtainable'<sup>(118)</sup>.

Why might anonymisation not be desirable in biobank research? Because the donors' traceability may be necessary for research in certain diseases. On the other hand, another important question which arose during the project was whether it was possible to obtain the complete anonymity of tissue samples. Some experts suggested that this is challenged by the possibility of genetic analysis, which allows for individual identification<sup>(118)</sup>.

Taken together, the contributions of the workshops suggested that the coding of samples (i.e. the code-key is not accessible for the researchers who work with the samples, but

kept separately by an authorised person or body) emerged as an important means of privacy protection in the field of human tissue and biobank research<sup>(118)</sup>.

Answers to these questions remain for future discussion and should be agreed in the following years, in order to enable the use of donor data in a legal, safe and secure manner across Member States.

#### IV. Research using biobanks <sup>(112)</sup>

The significance of biobank research is widely acknowledged in Europe: many countries, including the United Kingdom, Sweden and Estonia, have established national biobanks, and the number of local and small-scale biobanks is also increasing.

However, there is a regulative diversity in biobanking among Member States. For example, some countries, such as Sweden and Spain, have enacted discrete laws on biobanking. Others address this in a wider legal framework comprising research on human tissue (the United Kingdom, for example), and other countries, in the absence of particular regulations, derive their rules from European guidelines and statutes.

Despite this regulative diversity, however, some common standards can be observed. For example, participants in biobank research have the right to be kept informed about the use of their samples and data. Furthermore, the consent of the donor is obligatory in most countries. Also, donors have the right to withdraw from participation.

#### The Tiss. EU project provides free access to its website

The website of the Tiss.EU project (<http://www.tisseu.uni-hannover.de>) is still available and hosts an extensive database of documents on human tissue and biobanking to facilitate further research in the field. During its term, the Tiss.EU project also set up a network of experts in the field of human tissue research, which is also available on the project's website<sup>(116)</sup>.

<sup>(116)</sup> [www.tisseu.uni-hannover.de/index.php?option=com\\_peoplebook&Itemid=49](http://www.tisseu.uni-hannover.de/index.php?option=com_peoplebook&Itemid=49)

The Tiss.EU project organised nine international workshops and three International Status Conferences during the project period. The documents generated can be found on the project's website<sup>(117)</sup> and the revised reports have been published in a volume entitled *The Ethical and Legal Regulation of Human Tissue and Biobank Research in Europe*<sup>(118)</sup>.

As the number of repositories that can be linked increases and samples and data can be more easily transferred across country borders, the value of biobank research increases. This is why the Tiss.EU initiative was an important step in promoting human tissue and biobank research.

---

<sup>(117)</sup> [http://www.tisseu.uni-hannover.de/index.php?option=com\\_content&task=view&id=68&Itemid=44](http://www.tisseu.uni-hannover.de/index.php?option=com_content&task=view&id=68&Itemid=44)

<sup>(118)</sup> [http://webdoc.sub.gwdg.de/univerlag/2011/tiss\\_eu\\_book.pdf](http://webdoc.sub.gwdg.de/univerlag/2011/tiss_eu_book.pdf)



### Further information:

Project website:

<http://www.tisseu.uni-hannover.de>

Cordis database:

[http://cordis.europa.eu/search/index.cfm?fuseaction=proj.document&PJ\\_RCN=10230075](http://cordis.europa.eu/search/index.cfm?fuseaction=proj.document&PJ_RCN=10230075)

### Project team:

Project Coordinator  
 University Medical Center Göttingen,  
 Tiss.EU Project Manager: Dr Christian Lenk  
 GERMANY  
 E-mail: [clenk@gwdg.de](mailto:clenk@gwdg.de)  
 Tel. +49 551394186

### Project partners:

- University of Hannover, Medical Law and Bioethics Research Group, Centre for Philosophy and Ethics of Science, Germany
- University of Birmingham, Centre for Global Ethics, United Kingdom
- Stockholm University, Stockholm Bioethics Centre, Sweden
- Central European University Budapest, Center for Ethics and Law in Biomedicine, Hungary
- Fondazione Lanza, Padova, Center of Advanced Studies and Research in Ethics, Bioethics, Environmental Ethics and Social Issues, Italy
- Dublin City University, Institute of Ethics, Ireland
- Centre National de la Recherche Scientifique, France
- Institute of Bio-Law, Legal Pathways i.O., Aerdenhout, the Netherlands
- Vilnius University, Dept. of Medical History and Ethics, Lithuania

### EU contribution

This project has received co-funding from the European Union in the framework of the **7<sup>th</sup> Framework Programme** (Grant: 202204).

# Reprogramming the immune system for the establishment of tolerance (RISET)

*This project has received co-funding from the European Union in the framework of the 6<sup>th</sup> Framework Programme.*

The RISET acronym stands for reprogramming the immune system for the establishment of tolerance. RISET was a multinational project funded by the European Union under the 6th Framework Programme (a collection of actions at EU level to fund and promote research)<sup>(119)</sup>. During 66 months, from March 2005 to August 2010, the Université Libre de Bruxelles (Belgium) and the University of Oxford (United Kingdom) coordinated the RISET project, which brought together 26 partners from all over Europe to build a partnership between the academic and the private sector in the field of transplantation research.

Transplantation between individuals dramatically improves the survival of patients with an established organ failure. However, most patients who receive a transplant require taking powerful drugs for the rest of their lives, which suppresses their immune system. These drugs prevent the immune system from rejecting the transplanted organ but, on the other hand, they can cause serious health complications.

As time passes, immunosuppressive drugs can affect the health of transplant recipients, for example by increasing the risk of infections, malignancies, kidney problems or diabetes. On the other hand, there is a need for improving the standard of care in transplantation medicine, as some patients receive more immunosuppression than required, whereas others may not receive enough immunosuppression, which can cause damage in the transplant.

## Transplantation tolerance would represent a significant advance in medicine

Tailoring immunosuppressive drugs to each patient may be possible, according to recent scientific advances. Furthermore, the induction of transplantation tolerance may be another achievable goal. But what is transplantation tolerance? It is the focus of the RISET project, and could be defined as the state in which the immune system of the recipient of a transplant

accepts permanently the transplant in absence of chronic immunosuppression, so immunosuppressive drugs are not needed and the global functions of the immune system are preserved. To achieve transplantation tolerance would represent a significant advance in medicine.

## RISET: achieving transplantation tolerance by investigating innovative therapies

The goal of RISET was to design novel tools to determine and to induce transplantation tolerance. In this sense, the initiative aimed to translate advances in transplantation research into clinical practice and industrial development. Some of the achievements of RISET were the following.

### 1. The development of tests to predict tolerance

RISET developed new tests to predict transplant tolerance, some of them ready for commercial development in collaboration with the industry. These tests enable identifying transplant recipients who are truly tolerant or require minimal immunosuppression. This information is extremely useful as it indicates exactly how much immunosuppression each transplant recipient needs to take, which, in practical terms, reduces the amount of immunosuppressive drugs administered and, in consequence, their side effects.

According to one of the study groups of the project, *'it is hoped that these tests will lead to doctors being able to deliver more personalised care to transplant patients in future, by safely modifying the amount of medication patients take while preventing rejection of the donor organ.'* The new tests developed during the project can be consulted on the project website<sup>(120)</sup>.

<sup>(119)</sup> [http://ec.europa.eu/research/fp6/pdf/fp6-in-brief\\_en.pdf](http://ec.europa.eu/research/fp6/pdf/fp6-in-brief_en.pdf)

<sup>(120)</sup> <http://www.nds.ox.ac.uk/trig/research-overview/advanced-research-strategies-1/data-management-and-data-analysis>



<http://www.ont.es/publicaciones/Documents/RISSET%20NEWSLETTER%2009.pdf>

“*Transplantation tolerance would represent a significant advance in medicine.*”

## 2. Investigations to discover innovative therapies for transplantation tolerance

Some studies performed during the project period allowed to identify new genes and molecules relevant for the induction of transplantation tolerance. As an example, a Riset research group found that the tolerance of the recipient can be improved if a specific type of cell is transplanted along with the organ transplanted; these cells can ‘educate’ the immune system of the recipient in order to accept the new organ. Therefore, if the immune system of the patient receiving the transplant is educated not to reject the transplant, the need for immunosuppressive medicines will be reduced.

## 3. Development of a data repository

RISSET created a data repository to store clinical data and to follow-up patients in investigation studies about transplantation tolerance. According to the team involved in this work-package, ‘*integration of various sources of clinical data and of all the data produced during the experiments was the main task*’. This allowed to optimally exploit the clinical and biological data accumulated within the project in order to identify and validate biomarkers of tolerance.

The final report of the project defined this data repository as ‘*a unique resource on the follow-up of patients in tolerance investigation studies. A longitudinal visualisation tool, the LifeLines programme, allows representing both clinical and experimental data in a unified way and investigating the relationship between clinical events and test results in order to support the validation of biomarkers*’.

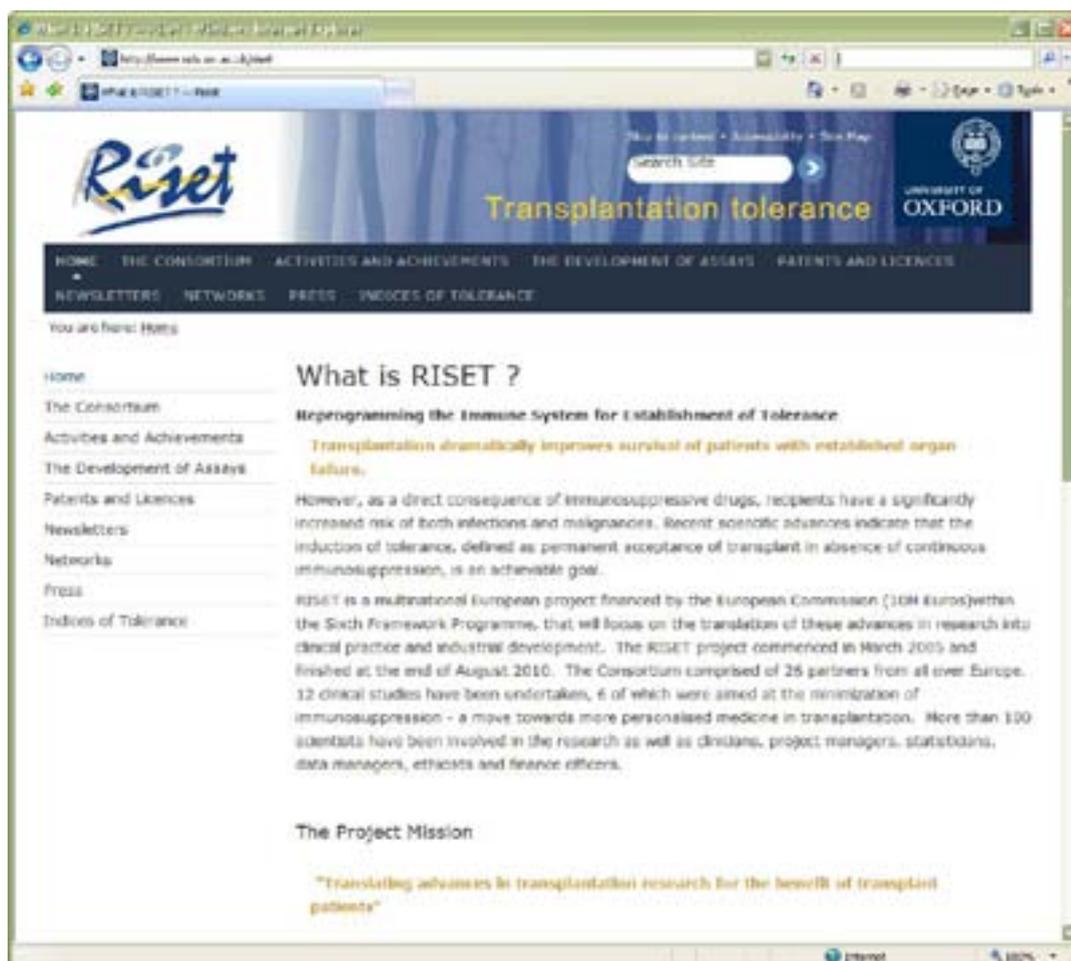
## 4. Ethical guidelines for clinical studies on tolerance induction

The project stimulated debate around the ethical aspects of tolerance induction, that allowed to achieve consensus on guidelines about this topic. The Riset ethics team produced a set of ethical recommendations on pilot clinical studies for tolerance induction, in particular focusing on the following topics: biomarker validation, the inequality of access to transplantation and the novel accompanying therapies across Europe.

According to V. Commin and A. Cambon-Thomsen, researchers of the project, a set of ten specific recommendations for clinical pilot studies on ethical aspects of tolerance induction was validated within the Riset consortium. Before being published, these recommendations were submitted for comments to various experts, committees, institutions and other stakeholders.

## 5. Educational programmes on transplantation tolerance

RISSET contributed to the development of educational materials on transplantation tolerance to distribute among patients and their families,



Project webpage at: <http://www.nds.ox.ac.uk/riset>

physicians, scientists, nurses and the media. Moreover, educational events about the ethical and regulatory frameworks on transplantation tolerance were organised for medical law and transplantation professionals, as well as for young researchers.

The RISET project captured international attention. According to RISET, the project appeared in the international press many times. In 2007, for instance, several articles were written following a press conference given at the RISET meeting in Madrid entitled 'Molecular signatures in transplantation tolerance'.

## 6. Understanding the way transplanted patients and the general public perceive tolerance induction

RISET analysed the state of public debate on immunosuppression and tolerance induction in five Member States (France, Netherlands, Belgium, Germany and Italy) in order to understand the way transplanted patients and the general public perceived tolerance induction. This analysis revealed an existing paradox: although there was an array of information on immunosuppressive drugs, transplant patients felt there was lack of information regarding what they were concerned. According to Christiane Kapitz and Anne Cambon-Thomsen, leaders of this work package, *'transplant patients have a common interest in their treatment, not met by the information from institutions or associations'*. As the RISET team concluded, *'thought needs to be given as to the type of information that might reduce the anxiety of patients for whom a transplant means dependence on drugs for life'*. The complete report of this survey is available on the project website.

### **RISSET performed an intense dissemination of the project outputs by publishing over 160 publications in international journals**

As part of its dissemination strategy, RISSET generated over 160 publications in international journals, several book chapters, and its findings were discussed at congresses, meetings and training events. The final findings were presented on 22 June 2010 at a symposium in the European Parliament (Brussels). The project website, which continues to be available, informs about the project, its activities and main achievements.

RISSET and the Immune Tolerance Network<sup>(121)</sup>, an international clinical research consortium, signed a collaboration agreement to exchange scientific results and biological samples. The Immune Tolerance Network is an international collaboration of researchers, which shares a similar mission with RISSET, that is, to accelerate the clinical development of immune tolerance therapies.

### **A competitive European task force to translate transplantation tolerance into clinical practice**

New treatments usually require years of research and development in the laboratory before they bring real benefits to patients. The RISSET consortium has sped up this process by building a partnership between researchers, clinicians and pharmaceutical companies to work together to achieve the transplantation tolerance. This was an ambitious goal but the outputs of RISSET are promising and suggest that an important step has been done to prevent organ rejection.

Although transplantation tolerance is far from being achieved, the RISSET network has contributed to advance towards this ultimate goal. The European Union provided not only the financial support but also the visibility needed to bring the project to success.

---

<sup>(121)</sup> [www.immunetolerance.org](http://www.immunetolerance.org)



### Further information:

Project website

<http://www.ont.es/publicaciones/Documents/RISET%20NEWSLETTER%2006.pdf>

<http://www.ont.es/publicaciones/Documents/RISET%20NEWSLETTER%2007.pdf>

<http://www.ont.es/publicaciones/Documents/RISET%20NEWSLETTER%2008.pdf>

<http://www.ont.es/publicaciones/Documents/RISET%20NEWSLETTER%2009.pdf>

### Project team:

The Project Coordinators:

Nuffield Department of Surgery

University of Oxford (UOXF)

John Radcliffe Hospital

Headington, Oxford

OX3 9DU

UNITED KINGDOM

Tel. +44 1865221300

Fax +44 1865763545

Universite Libre de Bruxelles (ULB)

Institut d'Immunologie Medicale

Rue Adrienne Bolland, 8

6041 Gosselies

BELGIUM

Tel. +32 26509560

Fax +32 26509562

### Project partners:

- Charité Universitätsmedizin Berlin (CHARITE), Germany
- Centre Hospitalier de Nantes (CHUN), France
- Universite Rene Descartes (UDESCARTES), France
- Blasticon Biotechnologische Forschung GmbH, Kiel, Germany
- Centro Nacional de Trasplantes y Medicina Regenerativa (ONT), Madrid, Spain
- Deutsches Krebsforschungszentrum (DKFZ), Heidelberg, Germany
- Henogen S.A., Gosselies, Belgium
- Institut National de la Sante et de la Recherche Medicale, Toulouse, France
- Institute for Clinical and Experimental Medicine, (IKEM), Prague, Czech Republic
- Leiden University Medical Center (LUMC), The Netherlands
- King's College London (KCL), United Kingdom
- Miltenyi Biotec MACSmolecular Business Unit, Cologne, Germany
- ProImmune Ltd, Oxford, United Kingdom

### EU contribution

This project has received co-funding from the European Union in the framework of the **6<sup>th</sup> Framework Programme**.

## Strengthen and develop scientific and technological excellence in research and therapy of leukaemia (CML, AML, ALL, CLL, MDS, CMPD) by integration of the leading national leukaemia networks and their interdisciplinary partner groups in Europe (European LeukemiaNet)

*This project has received co-funding from the European Union in the framework of the 6<sup>th</sup> Framework Programme.*

Leukaemia is the cancer of the blood cells which are responsible for fighting infections (known as leukocytes). It represents a challenge for society, among other reasons because of its frequency in all age groups. Several European countries have achieved a leading position in leukaemia research and therapy, but there is no true European world leadership in this sense yet, mainly due to fragmentation of leukaemia research in Europe.

Today, the European LeukemiaNet (ELN) is a network of excellence integrating the leading European groups in management and research in the field of leukaemia. It was born as a multinational project funded by the European Union under its 6th Framework Programme. The project lasted 86 months, starting in January 2004 and finishing in February 2011. Coordinated by Heidelberg University (Germany), this project set up a network for research and patient care in the field of leukaemia. It brought together over 1 000 leukaemia specialists from

189 institutions in 38 countries, including Switzerland, Israel, the United States and Russia. According to Prof. Hehlmann, coordinator of the project, 'honouring the success of the European LeukemiaNet, the contract between the European Union and the European LeukemiaNet was extended beyond the regular period of 6 years until February 2011'<sup>(122)</sup>.

### Cooperation as the fastest path to making leukaemia a curable disease

*'Before the creation of the European LeukemiaNet, there were a number of pre-existing networks in Europe that were each individually developing diagnostic methodology, running clinical trials and producing management guidelines,' stated Prof. Hehlmann. 'In this context, the main goal of the European LeukemiaNet was to create an environment in which these organisations could work more closely together, to harmonise their efforts and bring their advances to a wider community in a more timely fashion. This would allow to overcome national fragmentation, and to achieve research and treatment goals that are not easy to accomplish by a single country on its own'<sup>(123)</sup><sup>(124)</sup>.*

With this aim, the European LeukemiaNet integrated the leading leukaemia research groups across Europe, the industry and small and medium-sized companies, and provided central management, information and communication structures for them.



Participating centres

<sup>(122)</sup> European LeukemiaNet, Seventh annual activity report.

<sup>(123)</sup> Hehlmann R, et al, Leukemia 2004;18(4):665–9.

<sup>(124)</sup> www.haematologica.org/content/96/1/156.long

Topic	Reference
CML management recommendations	Baccarani <i>et al.</i> , <i>Blood</i> 2006; 108: 1809-20 Heldmann <i>et al.</i> , <i>Lancet</i> 2007; 370: 340-50 Baccarani <i>et al.</i> , <i>J Clin Oncol</i> 2009; 27: 6041-51*
CML molecular monitoring	Miller <i>et al.</i> , <i>Leukemia</i> 2009; 19: 57-63* Hughes <i>et al.</i> , <i>Blood</i> 2006; 108: 28-37* Beaumont <i>et al.</i> , <i>Leukemia</i> 2006; 19: 25-30*
AML management recommendations	Döhner <i>et al.</i> , <i>Blood</i> 2009; 10: 115-453-474*
APL management recommendations	Sanz <i>et al.</i> , <i>Blood</i> 2009; 113: 1875-81*
APL molecular monitoring	Grignani <i>et al.</i> , <i>J Clin Oncol</i> 2009; 27: 3654-3658*
CLL guidelines	Hallek <i>et al.</i> , <i>Blood</i> 2008; 111: 5445-56*
CLL molecular and flow-cytometric monitoring	Ghia <i>et al.</i> , <i>Leukemia</i> 2007; 21: 1-3* Rawstron <i>et al.</i> , <i>Leukemia</i> 2007; 21: 356-64*
Evidence- and consensus-based European guidelines on MDS	ELN Homepage <a href="http://www.leukemia-net.org/content/leukemia/els/recommendations">http://www.leukemia-net.org/content/leukemia/els/recommendations</a> *
CMPD management recommendations (PV, ET, PMF)	Barosi <i>et al.</i> , <i>J Clin Oncol</i> ; in press**
Response criteria for ET and PV	Barosi <i>et al.</i> , <i>Blood</i> 2009; 113: 4828-33*
Definition of resistance and intolerance to hydroxyurea in PV and agnogenic fibrosis	Barosi <i>et al.</i> , <i>Br J Haematol</i> 2010; 148: 563-563*
Reference document for four- and five-color flow-cytometry	Arraizalet <i>et al.</i> , <i>Cytometry B Clin Cytom</i> 2010; 78: 4-10*
Flow-cytometry in MDS	van de Loosdrecht <i>et al.</i> , <i>Haematologica</i> 2009; 94: 1124-34*
Consensus morphology collection	ELN homepage: <a href="http://www.leukemia-net.org">www.leukemia-net.org</a> *
Proposals for standardization of cytogenetic analyses	Halerach <i>et al.</i> , <i>Genes Chromosomes Cancer</i> 2007; 46: 404-9*
FIP1L1-PCDFRA – recommendations for diagnosis & molecular monitoring	Josipovic <i>et al.</i> , <i>Blood</i> 2007; 109: 4035-40* Score <i>et al.</i> , <i>Leukemia</i> 2009; 23: 332-330*
WT1 PCR standardization	Cifoni <i>et al.</i> , <i>J Clin Oncol</i> 2009; 27: 5195-201*
Gene expression profiling recommendations	Kohlmann <i>et al.</i> , <i>Br J Haematol</i> 2008; 142: 802-7*
Microarray analyses guidelines	Staal <i>et al.</i> , <i>Leukemia</i> 2006; 20: 1305-92*
Transplant-associated microangiopathy recommendations	Eurata <i>et al.</i> , <i>Haematologica</i> 2007; 92: 95-109*
Stem cell transplantation recommendations	
- in CLL	Dreyer <i>et al.</i> , <i>Leukemia</i> 2007; 21: 12-7*
- in MDS	De Witte <i>et al.</i> , <i>Haematologica</i> 2006; 91: 250-6*
Recommendations for management of infections	
- Quinolone prophylaxis for bacterial infections in afebrile neutropenia	Bacaner <i>et al.</i> , <i>EJC Supplements</i> 2007 (Vol. 5, 5-12)*
- HSV, VZV and EBV	Styczynski <i>et al.</i> , <i>Bone Marrow Transplant</i> 2009; 43: 737-70*
- CMV, HHV-8, HHV-7 and HHV-6	Ljungman <i>et al.</i> , <i>Bone Marrow Transplant</i> 2005; 20: 737-740*
- Empirical antifungal therapy in febrile neutropenic patients	Marchetti <i>et al.</i> , <i>EJC Supplements</i> 2007 (Vol. 5, 32-42)*
- Primary antifungal prophylaxis	Martens <i>et al.</i> , <i>EJC Supplements</i> 2007 (Vol. 5, 43-48)*
- <i>Candida</i> and <i>Aspergillus</i>	Herbrecht <i>et al.</i> , <i>EJC Supplements</i> 2007 (Vol. 5, 49-55)*
- Vaccination in stem cell transplant recipients	Ljungman <i>et al.</i> , <i>Bone Marrow Transplant</i> 2008; 42: 217-49*

### Recommendations on the topics

#### The project's specific goals were:

- to establish central information, communication, education and management structures;
- to set up European leukaemia subnetworks and interdisciplinary platforms;
- to carry out clinical trials in order to discover and develop leukaemia therapies;
- to create a European registry for leukaemias in order to determine incidence and disease patterns across Europe;
- to standardise diagnostic procedures and therapies;
- to perform meta-analyses and evidence-based guidelines to facilitate decision-making.

According to Prof. Hehlmann, the European LeukemiaNet is a model of transnational cooperation. Working together successfully created a spirit of cooperation and mutual trust<sup>(124)</sup>. The most visible results of the network were:

- the cooperative research projects and trials performed as reflected in a large number of high impact publications;
- the guidelines and management recommendations produced for each type of leukaemia;
- the European LeukemiaNet's website<sup>(125)</sup>, which has become a leukaemia information centre for physicians, patients, caregivers and the general public.

(125) [www.leukemia-net.org/](http://www.leukemia-net.org/)

## European registries for leukaemias

The European LeukemiaNet initiated public-private partnerships with the industry to enable the creation of multinational registries. This can be illustrated by the European Myelodysplastic Syndrome Registry (EUMDS Registry)<sup>(126)</sup>, where more than 650 patients have been registered so far. Another relevant example is the European Treatment and Outcome Study (EUTOS) for chronic myeloid leukaemia<sup>(127)</sup>, started in June 2007, which aims to improve understanding, promote best practices and enhance treatment outcomes of patients with chronic myeloid leukaemia.

## Research projects and trials in leukaemia

The European LeukemiaNet coordinated and facilitated the performance of pan-European clinical trials. As a consequence, new drugs for the treatment of leukaemia are under study (such as nelarabine or herceptin), and a number of joint European trials are ongoing. As an example, the first joint European trial with a promising drug for the elderly with a specific type of acute lymphoblastic leukaemia was started.

Another good example of the potential of networking is provided by the MILE study (Microarray Innovations in Leukemia study), which involves 11 laboratories (seven from European LeukemiaNet, three from the United States and one from Singapore) and that has already integrated data from more than 3 300 patients to reveal new patient subgroups with specific prognosis and survival.

## Guidelines and management recommendations

According to the seventh annual activity report of the project *'the European LeukemiaNet published over 35 guidelines and management recommendations on leukaemia diagnosis and therapy. These are the basis for high quality patient care in leukaemia across Europe'*<sup>(122)</sup>. In this sense, recommendations for virtually every leukaemia and interdisciplinary speciality were produced, such as recommendations on the management of

patients with neutropenia after intensive chemotherapy. These guidelines are helping healthcare professionals in performing their work and are contributing for the homogeneous management of patients with leukaemia across Member States.

## Input for development of new legislation on clinical trials

The European LeukemiaNet in collaboration with other European societies started an initiative to revise the Clinical Trials 2001/20/EC Directive<sup>(128)</sup>, which regulates clinical trials in the European Union. A document was produced which placed a focus on the specific negative effects of this directive on independent trials, that is, trials not sponsored by the pharmaceutical industry. This topic is of very high relevance because independent trials are very common in leukaemia research. Furthermore, detailed suggestions were provided to improve the legislation on clinical trials. More information about this initiative is available on the website of the project<sup>(129)</sup>.

*“The European LeukemiaNet improved leukaemia research and management across Europe.”*

## The European LeukemiaNet website received 48 000 visits in 2010

During the project, the European LeukemiaNet made the results of the network available for institutions, scientists, clinicians and patients' organisations. The knowledge generated was shared through annual symposiums, scientific sessions and workshops at international congresses. Seven annual symposiums of the European LeukemiaNet were held during the project<sup>(130)</sup>. As an example, the 7th Annual Symposium in Mannheim (Germany) was attended by over 450 participants from 33 countries<sup>(131)</sup>.

<sup>(128)</sup> Directive 2001/20/EC — 'on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use'.

<sup>(129)</sup> [http://www.leukemia-net.org/content/international\\_trials/index\\_eng.html](http://www.leukemia-net.org/content/international_trials/index_eng.html)

<sup>(130)</sup> [www.leukemia-net.org/content/home/el\\_n\\_symposia/agendas/](http://www.leukemia-net.org/content/home/el_n_symposia/agendas/)

<sup>(131)</sup> [www.leukemia-net.org/content/home/el\\_n\\_symposia/agendas/#e8151](http://www.leukemia-net.org/content/home/el_n_symposia/agendas/#e8151)

<sup>(126)</sup> [www.eumds.org](http://www.eumds.org)

<sup>(127)</sup> [www.eutos.org/content/home](http://www.eutos.org/content/home)

Although the project was by definition limited in time, the purpose was to make the dissemination of knowledge sustainable. With this aim, the website of the European LeukemiaNet<sup>(125)</sup> continues to actively place its knowledge at the disposal of physicians, patients, caregivers and the general public. The information is available in different European languages and includes a variety of resources, such as meetings, conferences, clinical trial registries, news, guidelines, printed materials, lists of patients' organisations, etc. In 2010 only, the European LeukemiaNet website received around 48 000 visits from 148 countries; this indicates the further need for such a knowledge tool.

### A network with great perspectives

February 2011 was the last month of European Union funding within the 6<sup>th</sup> Framework Programme, but not the last month of the European LeukemiaNet. Since then, the European Science Foundation<sup>(132)</sup> is funding the initiative and will continue this support until 2015.

Moreover, the European LeukemiaNet Foundation<sup>(133)</sup>, a charitable non-profit organisation, is

already supporting the European LeukemiaNet to address disparities in both access to treatment and quality of care, as well as to improve the care of leukaemia patients in Europe and globally. According to Prof. Hehlmann, Chairman of the European LeukemiaNet Foundation, this foundation 'offers access to an alliance of researchers, industry, politicians, patient groups and the medical profession to better understand origin and course of leukaemia and to reinvigorate the clinical development of new strategies and drugs'<sup>(134)</sup>.

The European LeukemiaNet is expanding and making the fragmentation of leukaemia research and management in Europe an issue of the past. According to the last activity report of the project, 'The European LeukemiaNet facilitated for more than 8 years cooperative research in a network of excellence, including over 1 000 leukaemia specialists from 182 institutions in 34 countries across Europe. The European Leukaemia Net has become a landmark in the medical history of leukaemia'<sup>(122)</sup>.

For a detailed description of the achievements and perspectives of the European LeukemiaNet, please read the article written by the project consortium<sup>(124)</sup>.

---

<sup>(132)</sup> [www.esf.org/](http://www.esf.org/)

<sup>(133)</sup> [www.elnfoundation.org/content/home/](http://www.elnfoundation.org/content/home/)

---

<sup>(134)</sup> [www.elnfoundation.org/content/about\\_us/words\\_of\\_the\\_chairman/](http://www.elnfoundation.org/content/about_us/words_of_the_chairman/)



### **Further information:**

Project website

[http://www.leukemia-net.org/content/home/index\\_eng.html](http://www.leukemia-net.org/content/home/index_eng.html)

[www.leukemia-net.org/](http://www.leukemia-net.org/)

### **Project team:**

175 participating centres in 33 countries (1 000 researchers and associates) are cooperating in the European LeukemiaNet, the complete list is available here:

[http://www.leukemia-net.org/content/home/the\\_project/participants/e7552/infoboxContent8345/ELN-ParticipantsStand05\\_2010.pdf](http://www.leukemia-net.org/content/home/the_project/participants/e7552/infoboxContent8345/ELN-ParticipantsStand05_2010.pdf)

### **EU contribution**

This Network of Excellence has received co-funding from the European Union in the framework of the **6th Framework Programme**.

# Transplantation Research Integration across Europe (TRIE)

*This project has received co-funding from the European Union in the framework of the 6<sup>th</sup> Framework Programme.*

The TRIE acronym stands for Transplantation Research Integration across Europe. This initiative was a multinational project funded by the European Union under the 6<sup>th</sup> Framework Programme. During 24 months, from March 2007 to February 2009, TRIE brought together academic, clinicians, industry and patient groups with the aim of developing a coherent and common strategy to define the future priorities of transplantation research in Europe. The project was coordinated by Université Libre de Bruxelles (Belgium).

Our immune system protects our body from foreign substances. People who receive transplants run the risk that their immune system rejects the transplant and causes the transplant to fail. For this reason, these patients must receive immunosuppressive drugs, which prevent their immune system from rejecting the transplant. However, the rejection of donor organs remains a serious problem for transplant patients; this is why further research is required to improve their long-term perspective.

Recent developments have opened new exciting perspectives for cell and organ transplantation, including the development of novel immunosuppressive agents, new diagnostic tools and validation of biomarkers to predict both transplant rejection and transplant tolerance. Transplant tolerance is an important issue for transplant patients. It can be defined as the state in which the immune system of the recipient of a transplant accepts permanently the transplant in absence of chronic immunosuppression, so immunosuppressive drugs are not needed and the global functions of the immune system are preserved.

## TRIE: defining the priorities of transplantation research in Europe

The overall aim of TRIE was to identify important questions in the field of transplantation research, focusing on themes for which joint efforts across multiple centres and countries in Europe would represent an added value. TRIE's objectives were:

- to identify current opportunities and challenges in the field of transplantation research;
- to suggest priority actions to be implemented in order to foster integration of research activities on transplantation.

The TRIE initiative worked on the identification of priority topics on cell and organ transplantation for further investigation. The selection of these priority topics was based on three sources: a dedicated Advisory Council chaired by Prof. Kathryn Wood from the University of Oxford, a large electronic survey among 370 key stakeholders (responses collected from 16 European Union countries, the United States and Canada), and a high level workshop in London gathering input from 60 leaders in the transplantation field.

This forum was open to involvement of any organisation or individual with a direct interest in transplantation research, e.g. National Societies for Solid Organ, Cell and Bone Marrow Transplantation, political representatives, research agencies and funding bodies, industry, patient organisations, etc<sup>(135)</sup>.

The project team synthesised all these contributions. Finally, consensus was reached on the following three priority topics for future initiatives in transplantation research<sup>(136)</sup>.

*Topic 1 — The identification of biomarkers in the donor and in the recipient which could help doctors to define risk profiles for patients and tailor pre- and post-transplant therapies*

A biomarker is a biological parameter that can be measured to predict a condition. In the context of transplantation, it could be used to predict how the recipient will respond to the transplantation, for example if the patient will be tolerant to the transplant received. This information is useful as it would indicate how much immunosuppression each transplant recipient needs to take, which, in practical terms, will

<sup>(135)</sup> [www.ont.es/publicaciones/Documents/RISET%20NEWSLETTER%2008.pdf](http://www.ont.es/publicaciones/Documents/RISET%20NEWSLETTER%2008.pdf)

<sup>(136)</sup> The TRIE (Transplantation Research Integration across Europe) project, Final report.

allow to reduce the amount of immunosuppressive drugs administered and, in consequence, their side effects.

*Topic 2 — The development of novel cell-based therapies for transplantation*

Cell-based therapies are treatments containing viable cells. These highly innovative therapies have a high potential in the treatment of various diseases as they restore tissues when the body's own repair system is inadequate or absent. For this reason, the development of cell therapy products should be taken into consideration as they might have positive implications for the transplantation process.

*Topic 3 — The establishment of innovative training programmes for scientists and healthcare staff involved in research on transplantation*

TRIE also undertook a comprehensive review of existing training resources in the field of transplantation in Europe<sup>(137)</sup>.

### TRIE formulated specific recommendations to address problems that cannot be solved independently

For each priority topic the TRIE consortium defined a number of specific recommendations.

*Topic 1 — The identification of biomarkers in the donor and in the recipient which could help doctors to define risk profiles for patients and tailor pre- and post-transplant therapies:*

- develop standardised tests and techniques to achieve an agreement on valid biomarkers among the transplantation community;
- in cooperation with the industry identify clinical trials that look at biomarkers using validated assays in multicentre studies;
- set up uniform biobanking facilities and data collection procedures to compare patient data across countries;
- develop biostatistics facilities and competencies to facilitate data analysis;

- envisage public-private partnership models to implement this topic;

- address ethical and regulatory considerations.

*Topic 2 — The development of novel cell-based therapies for transplantation:*

- standardise cell therapy protocols in order to improve regulatory issues and industrial investment in this field;

- involve industry to guarantee that products will be translated into clinical application in a later phase.

*Topic 3 — The establishment of innovative training programmes for scientists and healthcare staff involved in research on transplantation:*

- set up a coordinated network with identified high quality training centres; in association with the scientific societies and the industry, this network will contribute to integrate training needs in the transplantation research and facilitate the transmission of developments in the pharmaceutical industry to the clinical setting and vice versa;

- set up a platform to promote scientific collaboration among the transplantation community (staff exchange, promotion of techniques, discussion on projects, etc.).

### Greater collaboration with the industry is required to accelerate the development of therapies for transplantation

It was agreed that a closer collaboration with the industry is needed to ensure that the patients are the final beneficiaries of research progress. For this reason, members of the Innovative Medicines Initiative Joint Undertaking (IMI JU)<sup>(138)</sup> were invited to discuss the opportunities to speed up the development of better and safer medicines for patients in this field.

<sup>(137)</sup> [www.ont.es/publicaciones/Documents/RISET %20NEWSLETTER %2008.pdf](http://www.ont.es/publicaciones/Documents/RISET%20NEWSLETTER%2008.pdf)

<sup>(138)</sup> [www.imi.europa.eu](http://www.imi.europa.eu)

## Future actions derived from the TRIE initiative

The TRIE consortium organised a high level meeting entitled *Integrating transplantation research in Europe: perspectives for public-private partnerships*, which was held in Brussels on 3 November 2008, just a few months before the end of the project. During the meeting, the conclusions, recommendations and future perspectives emerging from the TRIE initiative were highlighted to policymakers, scientists, industry and patient representatives.

According to the final report of the project, several opportunities were being explored at the end of the project to ensure that these recommendations would be implemented in the form of concrete projects bringing scientists, clinicians and the industry more closely together with the ultimate goal of benefiting patients. Moreover, as stated by the project team, the TRIE initiative was open for consultation and

transplant patients, people waiting for transplants and patient organisations were requested to give feedback; early indications were that patients agreed with the priorities identified by the project partners <sup>(136)</sup>.

The EU-funded project TRIE aspired to develop a united strategy to define the future priorities of transplantation research in Europe. It coordinated clinicians, the academia, patient organisations and the industry to address issues jointly and effectively. The project identified key themes on cell and organ transplantation to foster novel clinical therapies.

This initiative was the first step to respond to specific questions that cannot be addressed independently but that require a scale of research across multiples centres and countries. If the recommendations provided are fully implemented, the European Union may become a leader in the field, thanks to the new synergies created.



### Further information:

Project website

[http://cordis.europa.eu/projects/rcn/86352\\_en.html](http://cordis.europa.eu/projects/rcn/86352_en.html)

### Project team:

Institut d'Immunologie Medicale  
Avenue F. D. Roosevelt 50  
1050 Brussels  
BELGIUM  
Tel. +32 71378560  
Fax +32 71378562  
E-mail: [mgoldman@ulb.ac.be](mailto:mgoldman@ulb.ac.be)

### Project partners:

- ABU International Project Management Limited, Ireland
- The Anthony Nolan Trust, United Kingdom
- The Chancellor, Masters and Scholars of the University of Oxford, United Kingdom
- Academisch Ziekenhuis Leiden, Netherlands

### EU contribution

This project has received co-funding from the European Union in the framework of the **6<sup>th</sup> Framework Programme**.

# Comparative analysis of medically assisted reproduction in the EU: regulation and technologies (SANCO/2008/C6/051)

*This service contract has been financed from the European Union in the framework of the Public Health Programme 2003–2008 (Call for Tender: SANCO/2008/C6/051).*

The European Society of Human Reproduction and Embryology (ESHRE)<sup>(139)</sup> was contracted by the European Union (DG SANCO)<sup>(140)</sup> in 2008 to outline the situation of fertility treatments in the European Union. The specific goals of the project were to compare among the European Union Member States:

- the different legal frameworks, as well as the eligibility and reimbursement criteria for fertility treatment;
- the current practices of fertility clinics.

## One out of six couples in Europe needs help conceiving

Infertility means not being able to conceive a baby within 12 months of regular unprotected sexual relations. Taking into account that one in six couples experience infertility problems at least once during their reproductive lifetime, infertility could be defined as a relevant problem.

There are treatments available to help women conceiving, often called fertility treatments or medically assisted reproduction. These include, for example, *in vitro* fertilisation (a process by which an ovum is fertilised by sperm outside the body), or intracytoplasmic sperm injection (*in vitro* procedure in which a single sperm is injected directly into an ovum). Around 5 million babies have been born worldwide since the first *in vitro* fertilised baby was born in 1978<sup>(141)</sup>.

Europe leads the field of medically assisted reproduction, initiating approximately 71 % of all reported treatments (Asia excluded)<sup>(139)</sup>.

However, it is not clear that all couples with fertility problems in the European Union receive

the best possible management, or that fertility treatment is accessible to all of them. Adequate implementation, legislation, reimbursement schemes and clinical practice in all the Member States are crucial to achieve this goal.

## Fertility treatment legislation in the then 27 EU Member States

According to a survey carried out for the project, 25 out of the then 27 EU Member States had already implemented the EU Tissues and Cells Directive<sup>(142)</sup> in 2006, and in most of them a Competent Authority<sup>(143)</sup> had started inspections of the fertility clinics. Moreover, 19 EU Member States reported to have specific legislation to regulate medically assisted reproduction in their countries, whereas eight countries reported to have only general legislation covering these kinds of procedures. There were national registries for the collection of clinical activities in more than 20 countries, and a few of them reported to have local registries as well. Regarding the establishment of national and local registries for donors, a clearly mosaic pattern among the European countries was detected<sup>(144)</sup>.

According to the project, the eligibility and reimbursement criteria for fertility treatments in the then 27 EU Member States varied, which implied that not all women in the European Union had the same access to treatment. Almost all EU Member States had some reimbursement scheme in place, but for many countries it was not clear which arguments had been used to decide on a restrictive policy. For example, in most countries the reasons for

<sup>(139)</sup> [www.eshre.eu](http://www.eshre.eu)

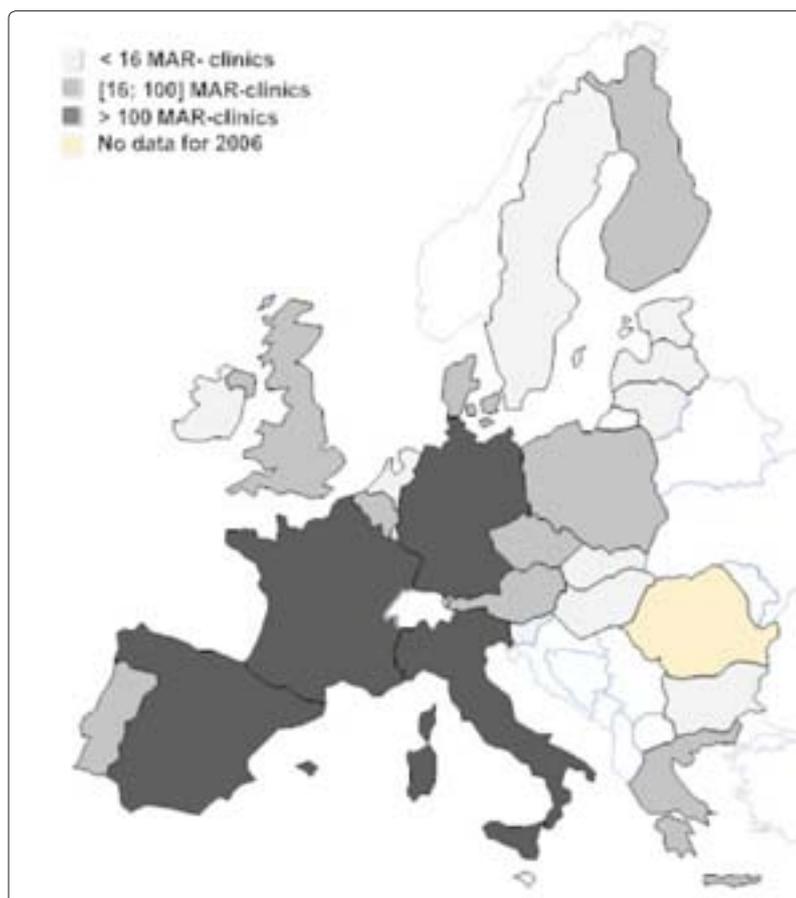
<sup>(140)</sup> [http://ec.europa.eu/dgs/health\\_consumer/index\\_en.htm](http://ec.europa.eu/dgs/health_consumer/index_en.htm)

<sup>(141)</sup> Assisted Reproductive Technology (ART) fact sheet. [www.eshre.eu/ESHRE/English/Guidelines-Legal/ART-fact-sheet/page.aspx/1061](http://www.eshre.eu/ESHRE/English/Guidelines-Legal/ART-fact-sheet/page.aspx/1061)

<sup>(142)</sup> Directive 2004/23/EC — ‘Setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells’.

<sup>(143)</sup> According to the Directive 2004/23/EC each Member State must nominate at least one Competent Authority, which is responsible for implementing regulatory activities in the field of human tissues and cells for transplantation and assisted reproduction.

<sup>(144)</sup> Comparative analysis of medically assisted reproduction in the EU: regulation and technologies. SANCO/2008/C6/051. Final report.



Geographical distribution of institutes for medically assisted reproduction (MAR) in the 27 EU Member States in 2006

restrictions on treatments were based on their cost-ineffectiveness, although in many cases the evidence base for this decision was weak. The eligibility criteria on reimbursement varied, with marital status and the maximum age of the mother being the factors that represented the most common limitations on access to a fertility treatment<sup>(144)</sup>.

### Characteristics of fertility clinics in the European Union

**Size and activity:** There were 971 clinics executing fertility treatments in the European Union in 2006, most of them located in Germany, France, Spain and Italy (with more than 100 clinics in each of them). Around 56 % of the Member States had less than 16 clinics. The size of the clinics varied considerably among the different countries<sup>(144)</sup>.

**Registries:** The EU Tissues and Cells Directive<sup>(142)</sup> introduced reporting and registration obligations for establishments performing fertility

treatments in the European Union; in this sense, recording activities (including procurement, testing, preservation, processing, storage and distribution) become compulsory, and these clinics must submit an annual report to the Competent Authority summarising their activities. Furthermore, the Competent Authority should maintain a National Registry for fertility clinics, specifying status on accreditation, authorisation and licensing. The project team highlighted that 21 of the then 27 Member States had established a National Registry already in 2009 (reporting was compulsory in 13 of them, and voluntary in the remaining eight countries). Moreover, around 60 % of EU countries had accreditation systems in place in 2006<sup>(144)</sup>.

### Outcomes of medically assisted reproduction:

In 2006, the number of fertility treatments carried out in the European Union approached 0.4 million (the 812 clinics surveyed reported a total of 374 986 treatment cycles performed that year). The mean number of treatments per million inhabitants varied among countries ranging from 120 to more than 2 000. The data collected show that more than 100 000 European citizens are born in the European Union as a result of fertility treatments. In some countries like Denmark and Slovenia, on average at least one child in every school class is the result of this kind of treatment<sup>(144)</sup>.

Looking at the success rates per country and per technique, the pregnancy rates after *in vitro* fertilisation ranged from 20 % to 30 % with similar rates between different countries. The same situation was repeated for intracytoplasmic sperm injection, which showed slightly increased pregnancy rates compared to *in vitro* fertilisation<sup>(144)</sup>.

### A substantial number of couples in the European Union travel to another country to obtain fertility treatment:

According to the project, the information available suggested that a substantial number of couples travel to another country to obtain medically assisted reproduction treatments. The main reasons for travelling abroad were the prohibition of the technique, the inaccessibility to the treatment due to the characteristics of the patients (such as age, sexual orientation or civil status), long waiting lists or high costs of the treatment in the country of origin. However, the project team highlighted that more elaborate research is necessary to obtain a complete picture of this phenomenon in Europe<sup>(144)</sup>.

## Registering key information within the field of medically assisted reproduction is still required

This study offered a first clear description of the situation of medically assisted reproduction in the European Union. However, according to the authors, there is still an urgent need in the Member States for registering key information within this field. The correct and precise collection of this data will improve quality and safety in medically assisted reproduction in Europe<sup>(144)</sup>.

The conclusions stated in the final report of this project highlighted that *'safety and quality are the main concerns when treating patients with medically assisted reproduction techniques. Adequate legislation, reimbursement schemes and good clinical practice are crucial to achieve this goal. Reliable data collection regarding the results obtained should allow improvement in the field'*<sup>(144)</sup>.

According to ESHRE, the ability to organise data collection covering most of the then 27 EU Member States was essential for this study<sup>(145)</sup>. ESHRE was recognised by the European Union as 'the expert' European organisation in the area of medically assisted reproduction. The collaboration of ESHRE with the European Union has improved the quality and safety of fertility treatments in the European Union. Nowadays, this collaboration continues to be active and fruitful.

The final report of this project is available in the website of DG SANCO<sup>(146)</sup> and ESHRE<sup>(147)</sup>.

---

<sup>(145)</sup> [www.eshre.eu/guidelines\\_and\\_legal/page.aspx/16](http://www.eshre.eu/guidelines_and_legal/page.aspx/16)

<sup>(146)</sup> [http://ec.europa.eu/health/blood\\_tissues\\_organs/docs/study\\_eshre\\_en.pdf](http://ec.europa.eu/health/blood_tissues_organs/docs/study_eshre_en.pdf)

<sup>(147)</sup> [www.eshre.eu/guidelines\\_and\\_legal/page.aspx/16](http://www.eshre.eu/guidelines_and_legal/page.aspx/16)



### **Further information:**

Project website  
<http://www.eshre.eu/>

### **Project team:**

The European Society of Human Reproduction and Embryology (ESHRE)  
Meerstraat 60  
1852 Grimbergen (Beigem)  
BELGIUM  
Tel. +32 22690969  
Fax +32 22695600

### **EU contribution**

This service contract has been financed from the European Union in the framework of the **Public Health Programme 2003–2008** (Call for Tender: SANCO/2008/C6/051).

## Analysis and comparison of testing methods and testing laboratories in the EU and third countries for the biological markers specified in the blood and tissues and cells Directives (SANCO/2008/C6/012)

*This service contract has been financed from the European Union in the framework of the Public Health Programme 2003–2008 (Call for Tender: SANCO/2008/C6/012).*

Medical therapies based on substances of human origin (blood, tissues, cells and organs) are increasingly common and save many lives. However, care must be taken to eliminate any risk of patients being infected with diseases such as hepatitis and HIV through such therapies. To ensure the quality and safety of blood, tissues and cells, all European Union Member States are obliged to comply with the standards laid down in EU legislation<sup>(148)</sup>.

One strategic aim of the European Union is to develop and implement an import/export instrument to assist Member States in the exchange of substances of human origin. To facilitate the achievement of this objective, the European Union (DG SANCO)<sup>(149)</sup> contracted ALCIMED to carry out a project over the course of 12 months, from January to December 2009. ALCIMED<sup>(150)</sup> is a biotechnology company based in Paris that had already participated in previous projects undertaken for the European Union.

The project's general goal was to facilitate the exchange of substances of human origin between Member States as well as between Member States and non-EU countries (hereinafter referred to as 'third countries'). This general objective was concretised by defining the following specific objectives:

- to understand the limitations in the exchange of substances of human origin between Member States as well as between Member States and third countries;
- to provide recommendations to facilitate the exchange of substances of human origin between Member States;
- to provide recommendations to facilitate the exchange of substances of human origin between Member States and third countries (with a focus on the United States).

“The Commission may consider these strategies and measures in its evolving political and economic context.”

*ALCIMED, Authorisation of testing laboratories, testing methods and kits for biological markers used in blood, tissue and cell establishments in the EU, A report to the Commission.*

ALCIMED conducted a bibliographical research of documents published on relevant websites. Patient organisations also provided information on the exchange of substances of human origin between countries and on the difficulties experienced. In addition, 38 key opinion leaders within Competent Authorities and within blood, tissues and cells establishments<sup>(151)</sup> were contacted directly to discuss these issues. Finally, a scientific experts' committee was established in collaboration with the European Commission for the verification of all technical aspects of the project.

The project team focused on the situation of five European Member States (the United Kingdom, France, Italy, Netherlands and the Czech Republic) and three countries outside Europe (the United States, Australia and Brazil).

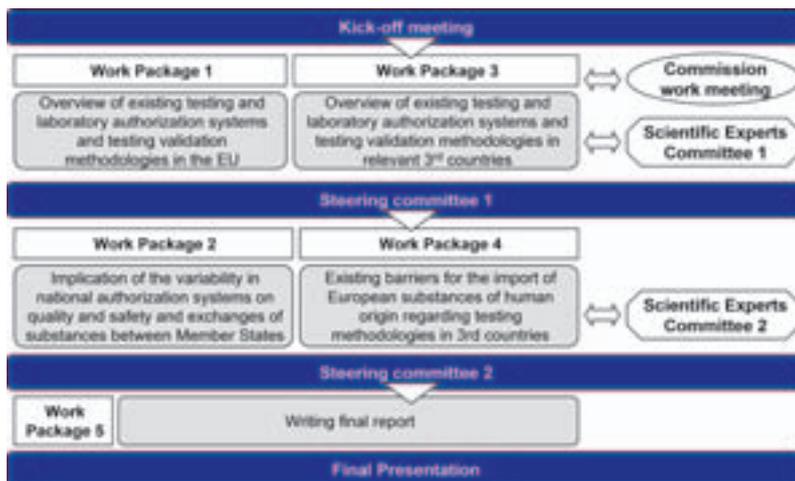
The first phase of the project (Work Packages 1 and 3), gave an overview of existing authorisation and validation systems and currently used diagnostic kits for blood, tissues and cells.

<sup>(148)</sup> [http://ec.europa.eu/health/blood\\_tissues\\_organs/policy/index\\_en.htm](http://ec.europa.eu/health/blood_tissues_organs/policy/index_en.htm)

<sup>(149)</sup> [http://ec.europa.eu/dgs/health\\_consumer/index\\_en.htm](http://ec.europa.eu/dgs/health_consumer/index_en.htm)

<sup>(150)</sup> [www.alcimed.com/](http://www.alcimed.com/)

<sup>(151)</sup> Blood, tissues and cells establishments are authorised centres that receive, test, process, store and distribute blood, tissues or cells (including gametes and embryos) for human application in the European Union.



Project structure

The second phase (Work Packages 2 and 4) identified the existing variability in different national authorisation and validation systems as well as in testing methods, and analysed its implication for the exchange of substances of human origin.

Finally, a substantial time of the project was spent to formulate the recommendations to the European Commission (Work Package 5).

### What factors hinder the exchange of substances of human origin between Member States in the European Union?

According to the final report of the project<sup>(152)</sup>, the following factors influence on the exchange of substances of human origin within the European Union.

- *The nature of the substance:* for instance, there is a growing need for the exchange of haematopoietic stem cells between countries, which has prompted the establishment of systems to facilitate the exchange of stem cells. On the other hand, the exchange of other cells, such as reproductive cells, is usually limited.

- *Self-sufficiency policies:* several European countries have declared self-sufficiency policies for blood and blood components. As a result, these countries do not exchange the regulated substances or only to a limited extent.

- *Differences in national testing requirements:* the European Directives set out minimal safety requirements for substances of human origin, which are followed by all Member States. However, the Directives allow any Member State to adopt additional safety measures, which in practice vary between Member States. Such differences can hinder the exchange of blood, tissues and cells.

- *Differences in national donation legislation:* the legislation that regulates donations of human blood, tissues and cells varies between Member States, which restricts the exchange of substances of human origin.

- *Lack of matching standards between Member States:* to a limited extent, new EU Member States reported problems in implementing the common quality and safety standards specified by the European Directives.

- *Lack of networking between establishments:* networks of trusted tissue establishments remain small and do currently not extend across the whole European Union.

According to the project's final report, the difficulties in the exchange of substances of human origin between Member States in the European Union do not arise through a lack in quality standards, but rather through differences in the regulatory environment. Therefore, regulatory issues should be the target to facilitate the exchange<sup>(152)</sup>.

<sup>(152)</sup> ALCIMED, Authorisation of testing laboratories, testing methods and kits for biological markers used in blood, tissue and cell establishments in the EU, A report to the Commission.

## What factors hinder the exchange of substances of human origin between Member States and countries outside the European Union?

The following difficulties were highlighted<sup>(152)</sup>.

- *Regulations limiting export:* third countries, such as Australia, have defined policies that ensure a sufficient supply of substances of human origin for the domestic population, which can lead to restrictions of exports to other countries.
- *Varying testing requirements:* third countries have reported difficulties in meeting all testing requirements of Member States which go beyond the requirements specified in the European Directives. On the other hand, third countries may specify testing methods that differ from the European practices.
- *Self-sufficiency policies:* Competent Authorities in third countries (e.g. Australia) prefer self-sufficiency policies to circumvent the need to test imported substances.
- *Remuneration of donations:* Member States of the European Union that ban remunerated donations cannot import substances of human origin from third countries that allow such remunerations.
- *Matching quality and safety standards:* particularly the United States does not consider their quality and safety standards to match with European standards, a fact that hampers severely the exchange of substances of human origin between the two zones. To overcome this barrier, according to the project, the focus should be put on these standards and on creating a common ground in the discussion between the United States and Europe.

- *Litigation risks:* the potential financial consequences of lawsuits in third countries prevent small private establishments in Member States from exporting blood, tissues and cells to such third countries.

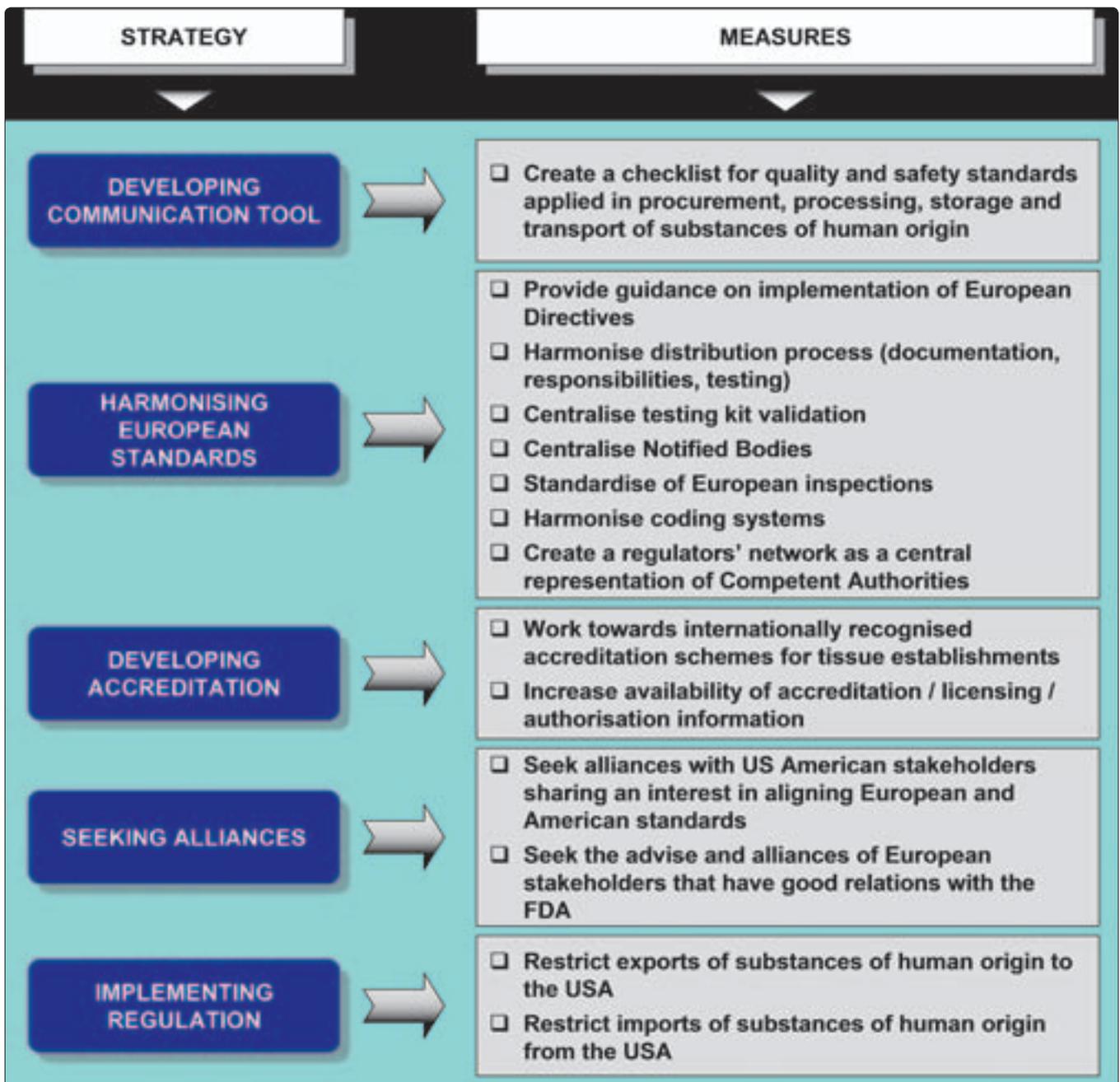
## How to facilitate exchange between Member States as well as between Member States and third countries

The following strategies and measures were suggested to facilitate exchange between Member States as well as between EU Members and third countries<sup>(152)</sup>.

- *Developing communication tools:* communication tools which bridge the gap between regulatory systems with different quality and safety requirements are currently the most developed measures to facilitate the exchange of blood, tissues and cells between countries.
- *Harmonising European standards:* according to the project team, the harmonisation of European standards has a dual function: it facilitates the exchange of substances of human origin between Member States and it strengthens the visibility of a European quality and safety standard. Third countries perceive this harmonisation of European standards as positive, which promotes the exchange. Several projects for the harmonisation of European standards are currently under way in the European Union.
- *Developing accreditation schemes:* an internationally recognised accreditation scheme for tissue establishments could facilitate the exchange of tissues between Member States and third countries. The benefits of such schemes have been demonstrated by similar initiatives for cells establishments such as JACIE ([www.jacie.org/](http://www.jacie.org/)).

- *Seeking alliances:* strong alliances with stakeholders in the United States and in Europe will facilitate an agreement with the United States on quality and safety standards for blood, tissues and cells, which, in the medium term, will facilitate the exchange of these products.
- *Implementing regulation of imports and exports:* the European Commission should seek negotiations with the US Food and Drug Administration (FDA) on a mutual acceptance of quality and safety standards.

The political and the economic context concerning substances of human origin is dynamic and has seen substantial regulatory changes and commercial developments in the last years. It is therefore important to consider this evolving context for the effective implementation of these recommendations.



**Project team:**

ALCIMED  
57, bvd de Montmorency  
75016 Paris  
FRANCE  
Tel. +33 144301741  
Fax +33 144304432  
<http://www.alcimed.com/>

**EU contribution**

This service contract has been financed from the European Union in the framework of the **Public Health Programme 2003–2008** (Call for Tender: SANCO/2008/C6/012).



# Organ donation and transplantation



The availability of donor organs is often a question of life and death for patients requiring a transplant. With transplantation now a commonplace technique, one of the main factors limiting the number of transplants is the shortage of organs.

The Communication on organ donation and transplantation adopted by the Commission in 2007, and the undertaken **impact assessment** identified major policy challenges for organ donation and transplantation. These included:

- ensuring the quality and safety of human organs,
- increasing organ availability,
- enhancing the efficiency and accessibility of transplantation systems in the European Union.

A public consultation demonstrated wide support for EU initiatives in this field.

### Action Plan and legislation

In December 2008, the Commission adopted a **proposal for a Directive** that defines quality and safety requirements for human organs intended for transplantation, and an Action Plan on Organ Donation and Transplantation (2009–2015) to support voluntary cooperation between Member States in this field.

Under this **Action Plan**, several European projects were funded via the Research and Health Programmes, to support the cross-border cooperation between Member States in the field of organ donation and transplantation, in particular to help increase organ availability and enhance the efficiency and accessibility of transplant systems at national and EU levels.

The Directive on standards of quality and safety of human organs intended for transplantation (Directive 2010/53/EU) was adopted by the European Parliament and the Council on 7 July 2010. It provides for the appointment of Competent Authorities in all Member States, for authorisation of procurement and transplantation centres and activities, for traceability systems and for the reporting of serious adverse events and reactions. Moreover, the Directive will set requirements for the safe transportation of organs and for the characterisation of every donor and organ. Member States were required to transpose the requirements of the Directive by

27 August 2012. Further to the transposition of the Directive, the European Commission is supporting the Member States in its implementation.

It is also foreseen in the ‘Mother Directive’ 2010/53/EU that **where organs are exchanged between Member States**, detailed rules for its uniform implementation should be adopted by the Commission regarding procedures:

- (a) for the transmission of information on organ and donor characterisation (for example type and size of organ, donor’s age, gender, health history);
- (b) for the transmission of the necessary information to ensure the traceability of organs (in compliance with confidentiality and data security measures);
- (c) for ensuring the reporting of serious adverse events and reactions (which allows the doctors to take appropriate measures if needed).

The Commission Implementing Directive 2012/25/EU laying down information procedures for the exchange, between Member States, of human organs intended for transplantation was adopted on 9 October 2012 and shall be transposed in national laws by 10 April 2014.

### Other cooperation activities

To raise the awareness of journalists from different EU countries on this important issue and to foster the exchange of best practices, the European Commission has been also organising yearly since 2010 a journalists’ workshop on organ donation and transplantation. These workshops involve speakers from various national authorities and other experts in the field.

The European Commission also has cooperation activities with key global partners such as the Council of Europe and the World Health Organisation, and European Organ Exchanges Organisations such as Eurotransplant and Scandiatransplant.

### Medical applications of organ transplantation

There are many types of organs that are currently being transplanted in order to cure multiple diseases, for example the following.

- **Kidneys** are the most frequently transplanted organs. Kidney transplantation is the organ transplant of a kidney in a patient with end-stage renal disease. Kidney transplantation is typically classified as deceased-donor (formerly known as cadaveric) or living-donor transplantation depending on the source of the recipient organ. As every deceased donor has two kidneys, two patients can be provided with a donor kidney. Living-donor renal transplants are further characterised as genetically related (living-related) or non-related (living-unrelated) transplants, depending on whether a biological (family) relationship exists between the donor and recipient.
- **Liver transplantation** is the replacement of a diseased liver with a healthy liver allograft. Liver transplantation nowadays is a well-accepted treatment option for end-stage liver disease and acute liver failure. In some cases, a liver can be split and therewith two patients can be provided with a new organ.
- **Heart transplantation** is performed on patients with end-stage heart failure or severe coronary artery disease. The most common procedure is to take a working heart from a recently deceased organ donor (allograft) and implant it into the patient. The patient's own heart may either be removed (orthotopic procedure) or, less commonly, left in to support the donor heart (heterotopic procedure).
- While **lung transplants** carry certain associated risks, they can also extend life expectancy and enhance the quality of life for end-stage pulmonary patients.
- A **heart-lung transplant** is a procedure carried out to replace both heart and lungs in a single operation. Due to a shortage of suitable donors, it is a rare procedure.
- A **pancreas transplant** involves implanting a healthy pancreas (one that can produce insulin) into a person who has diabetes. The healthy pancreas comes from a donor who has just died or it may be a partial pancreas from a living donor. At present, pancreas transplants are usually performed in persons with insulin-dependent diabetes who have severe complications.
- **Small bowel transplant** is still very rare but does take place in some EU Member States.

Treatments based on substances of human origin are dependent on citizens who are willing to donate organs. Citizens are all potential donors able to help patients in need, and in many cases donors are even able to save other people's lives.

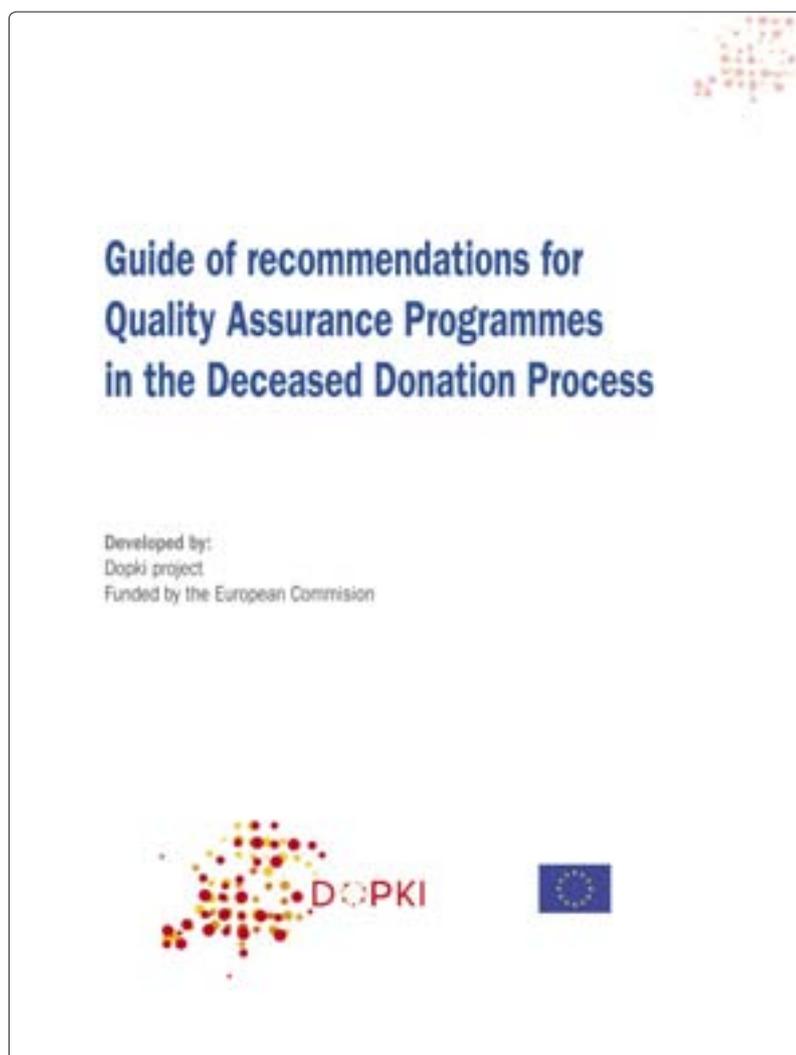
In the projects funded in this field under the EU Health Programmes as well as in its own activities and in its cooperation with the Member States' National Competent Authorities and other international partners, the European Commission is continuously supporting activities in the various and often complex issues related to organ donation and transplantation such as deceased donation and living donation, transplant systems and quality improvement methods, follow-up of transplanted patients and living donors, cross-border agreements to exchange organs or patients and communication activities.

## Overview of projects in this section

Acronym	Title	Page
DOPKI	Improving the knowledge and practice of Organ Donation	136
ALLIANCE-O	European Group for Coordination of National Research Programmes on Organ Donation and Transplantation	141
ETPOD	European Training Programme on Organ Donation	146
EULID	European Living Donation and Public Health	151
EFRETOS	European Framework for the Evaluation of Organ Transplants	156
ELIPSY	European Living Donor Psychological Follow-up	162
EDD	Developing Guidelines for the Organisation of a Public Organ Donation Day	166
ODEQUS	European Quality System Indicators and Methodology on Organ Donation	173
COORENOR	Coordinating a European Initiative among National Organisations for Organ Transplantation	177
ELPAT Conference	2nd Conference on Organ Transplantation: Ethical, Legal and Psychosocial Aspects — Expanding the European Platform	184
MODE	Mutual Organ Donation and Transplantation Exchanges: Improving and developing deceased organ donation and transplantation programmes (Joint Action)	188
ACCORD	Achieving comprehensive coordination in organ donation throughout the European Union (Joint Action)	193
	European Training Course for Trainers in Transplant Donor Coordination in the European Union	199
	Study on the set-up of organ donation and transplantation in the EU Member States, uptake and impact of the EU Action Plan on Organ Donation and Transplantation (2009–2015)	204
EULOD	Living Organ Donation in Europe	208

## Improving the knowledge and practice of Organ Donation (DOPKI)

*This project has received co-funding from the European Union in the framework of the 6th Research Framework Programme.*



Many patients cannot benefit from the improvements and advantages in transplantation medicine as less organs are available for transplantation than there are patients on waiting lists. Increasing the number of available organs for transplantation is a permanent challenge for healthcare systems throughout Europe and globally. A way forward to improve this situation is to maximise the potentials of deceased organ donation.

The main objectives of the DOPKI project were to improve knowledge and develop a common method to determine the potential for deceased organ donation and its likely outcome, and to define the limits of organ safety and quality. The project aimed to use the knowledge generated to give recommendation for the generation of actions that could help to improve deceased donation activities and ultimately donation rates.

A consortium of 13 organisations covering 16 European countries worked together in the project from January 2006 to March 2009. Project partner countries represented 80 % of the population and 80 % of all the donation and transplantation activities in Europe. DOPKI was coordinated by the Spanish National Transplant Organisation (ONT).

### Knowledge, tools and methods generated by DOPKI

**State-of-the-art overview on donation and transplantation practices and outcomes in DOPKI countries:** As one of the main outcomes of the project, DOPKI compiled a comprehensive overview of donation and transplantation practices and outcomes on the basis of data collection from the participating countries: *Report on the general European situation: technical, legal and socio-sanitary point of view*<sup>(153)</sup>. To support the comprehensive overview, a cross-sectional study exploring the relationship between donation rates and demographic, economic and healthcare factors that

*“Quality Assurance Programmes in the deceased donation process are essential internal tools for the countries, and if they are established under the umbrella of common definitions, they could be used to make international comparisons in the future.”<sup>(154)</sup>*

*Guide of recommendations for Quality Assurance Programmes in the Deceased Donation Process*

<sup>(153)</sup> [www.ont.es/internacional/Documents/DOPKI.pdf](http://www.ont.es/internacional/Documents/DOPKI.pdf)

could have an impact on donation rates were also investigated.

The overview showed considerable variation in donation and transplantation practices and outcomes in the studied European countries. Furthermore, the report highlighted an important barrier to measuring donor potential: *'One of the major problems when it comes to the analysis of donor potential is the lack of data ... Unless data collection is carried out according to standardised patterns it is very difficult to make comparisons between the countries.'*

**Common methodology to estimate the potential of deceased donation and evaluate the performance of the deceased donation process:** DOPKI partners have developed a common methodology to estimate the potential of the (at that time so-called) 'heart-beating' deceased donation and to evaluate the performance and global effectiveness of the deceased donation process and to identify areas for improvement.

In doing so, DOPKI partners defined a set of indicators and collected data from 30 hospitals throughout Europe who participated in the pilot study to validate the methodology. Based on the data, DOPKI developed a basic set of indicators in the following areas: potential of donation, areas of improvement and global effectiveness. Reference values were established for these indicators. A comparison of hospitals with this reference value helped identify areas of improvement in the deceased donation process.

Based on the pilot and knowledge exchange among project partners, DOPKI has developed a *Guide of recommendations for Quality Assurance Programmes in the Deceased Donation Process*<sup>(154)</sup> as one of the main outputs of the project. The report sets out a definition and objectives of a quality assurance programme in deceased donation process, gives an overview of the state of the art of quality assurance programmes in the deceased donation process in DOPKI countries and finally it provides general recommendations to build up quality assurance programmes. Such quality assurance programmes are expected to help the design and implementation of targeted actions to improve the donation process and tackle organ shortage.

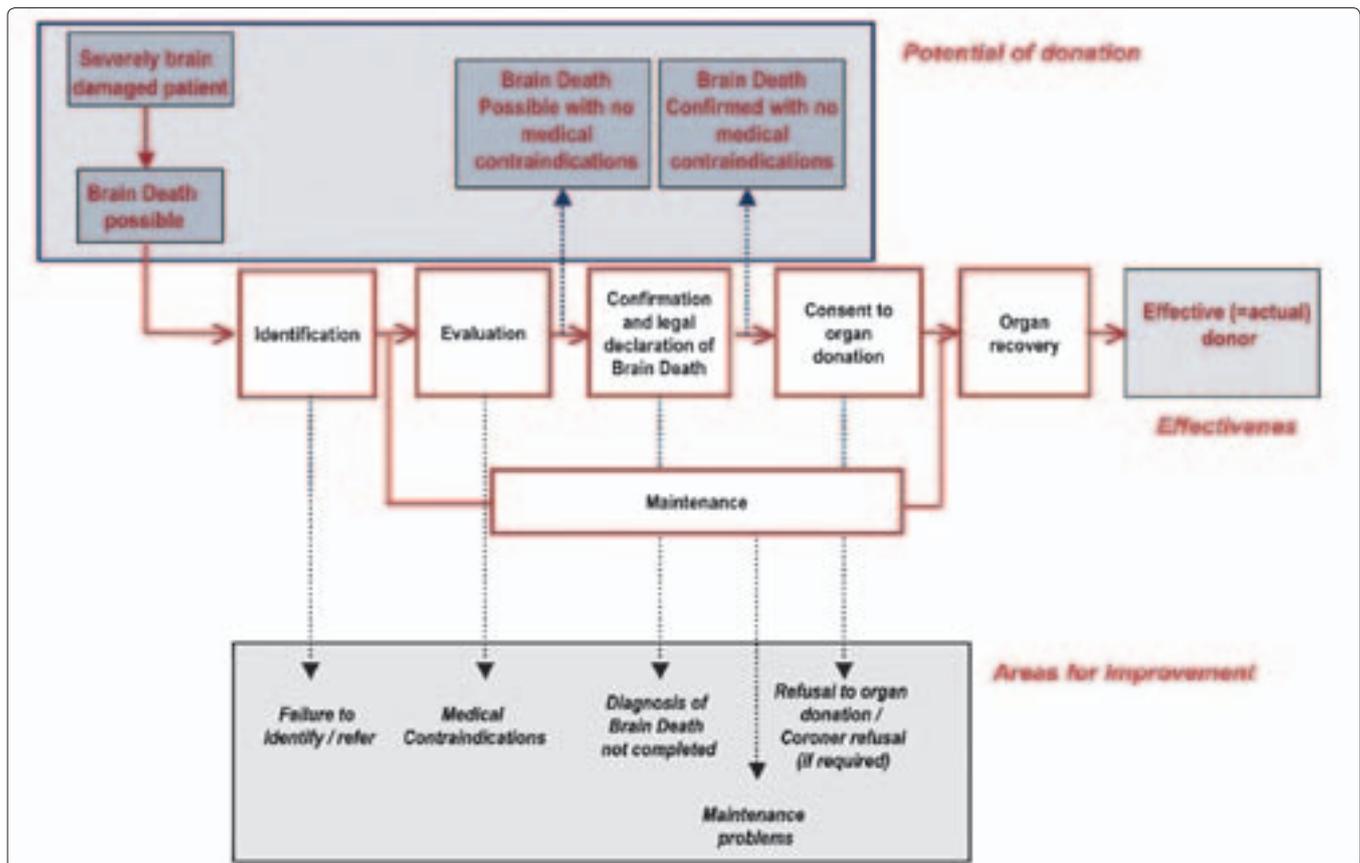
## THE NEED FOR QUALITY ASSURANCE PROGRAMMES IN THE DECEASED DONATION PROCESS

Since the first successful kidney transplantation was performed in 1954, organ transplantation has progressively become a healthcare practice of unequivocal importance. Kidney transplantation represents the best therapeutic option for patients with end-stage renal disease as it provides better outcomes in terms of survival, quality of life and cost-effectiveness than other renal replacement therapies. Liver, heart and lung transplantations represent an almost unique therapeutic alternative for patients with end-stage liver, heart and lung failure. The different modalities of pancreas transplantation have become a solution to re-establish insulin secretion in selected diabetic patients in order to improve patient survival and quality of life. Small bowel transplantation, usually performed as a part of a multi-organ transplantation, is still a relatively uncommon procedure, but one aimed at solving life-limiting conditions. Results of organ transplantation are excellent and have continued improving over the years, thanks to the advances in immunosuppression and the acquired experience and knowledge about surgical and medical procedures.

Despite these impressive advances, there are still many problems to be solved in the field of organ transplantation: grafts are mostly lost in the long term due to the so-called chronic rejection and death with a functioning graft, mainly due to cardiovascular disease. Furthermore, short- and long-term consequences of immunosuppression decrease organ recipients' longevity and quality of life. However, an even earlier obstacle has to be faced regarding organ transplantation, that is, the shortage of organs to cover the demand. The number of patients joining the waiting list has been progressively increasing over the years because of the excellent results of transplantation, while the number of donors and organs has not increased or has increased at a much lower rate. As a result, organs available for transplantation have not been keeping up with demand. In the European Union (EU), 57 343 patients were waiting for a kidney, a liver or a heart transplant at the end of the year 2007, while only 25 932 kidney, liver or heart transplant procedures were performed during that entire year. Similar figures can be found all over the world, thus making organ shortage a worldwide problem. In addition to the problem of organ shortage for transplantation, it is apparent that donation and transplantation activities differ among the countries in general terms, and among EU countries, in particular. This means that the effectiveness of our systems to face organ shortage is highly variable, which subsequently means high variability regarding donation and transplantation activities and therefore the possibilities of transplantation for EU citizens.

*Guide of recommendations for Quality Assurance Programmes in the Deceased Donation Process*

<sup>(154)</sup> <http://www.ont.es/publicaciones/Documents/DOPKI%20GUIA.pdf>



General approach to the process of deceased donation after brain death (Guide of recommendations for Quality Assurance Programmes in the Deceased Donation Process)

### DOPKI Registry for Expanded Criteria Donors

Based on the DOPKI definitions, the project created a registry of harmonised information from donors and recipients on outcome and survival. An internal web-based registry with high safety levels was created and made accessible to project partners who could upload the information on expanded criteria donors and the outcome of their recipients. The information was analysed as a first approach on the use of expanded criteria donors. By doing so, the project has managed to take the necessary first steps to provide a basis for developing quality and safety guidelines for using such donors.

### DOPKI tool to estimate cost-effectiveness of organ donation programmes

The project designed a statistical model that helped to estimate the present net value cost savings and additional quality-adjusted life years (QALY) in renal transplantation that occur as the result of improved organ donation

activities<sup>(155)</sup>. In addition to the model, the tool includes a Model User Guide and a Literature Review with published input variables. The model was developed for participant organisations of the DOPKI project in a way that it can be adapted to any DOPKI countries and it is able to capture the social value of other solid organ transplants. Additionally, the first country adaptation was completed in Hungary during the project's lifetime.

In order to disseminate its results, the DOPKI project organised a final conference on 24 March 2009 in Madrid to various stakeholders. DOPKI maintained a website during the project's lifetime<sup>(156)</sup>. Two DOPKI newsletters and a DOPKI leaflet helped to spread the information about the project and its results in the beginning and at the end of the project<sup>(157)</sup>.

<sup>(155)</sup> DOPKI Newsletter 2009: <http://www.ont.es/publicaciones/Documents/DOPKI%20NEWSLETTER%202009.pdf>

<sup>(156)</sup> The main reports and the Guide are available on the Spanish National Transplant Organisation, [www.ont.es](http://www.ont.es)

<sup>(157)</sup> DOPKI Newsletter 2007: <http://www.ont.es/publicaciones/Documents/DOPKI%20NEWSLETTER%202007.pdf>; DOPKI Newsletter 2009: <http://www.ont.es/publicaciones/Documents/DOPKI%20NEWSLETTER%202009.pdf>

The scientific community in organ donation and transplantation have been reached by presentations on national and international conferences and via scientific publications. Cooperation with other EU-funded projects in the same field was maintained throughout the project's lifetime.

Results of the project were channelled through a link created with the WHO via the Global Observatory on Donation and Transplantation<sup>(158)</sup>, an observatory developed by the Spanish National Transplant Organisation in cooperation with the WHO. The link allowed a bilateral information flow. Information was available on donation and transplantation activities and organisational issues in Europe and in other WHO regions. At the same time, this was an opportunity to disseminate the knowledge and recommendations generated by the DOPKI on these issues.

The link with the WHO represented a unique opportunity to cooperate with the initiative 'Data harmonisation in transplantation: measuring the potential supply of organs from deceased donors' organised by the WHO.

the Transplantation Society and the Spanish National Transplant Organisation. The initiative aimed to agree on a common methodology to estimate the potential of donation and prospectively identify potential deceased organ donors. The experience of DOPKI supported the development of this global initiative.

“DOPKI is about why and what. Why aren't there enough organs? What can we do to improve that?”

*Guide of recommendations for Quality Assurance Programmes in the Deceased Donation Process*

The DOPKI project developed knowledge and tools that in the future can help to increase deceased donation rates and hence transplantation activities. These tools help improve the way health systems tackle the universal and dramatic problem of organ shortage. The definitions and knowledge generated by DOPKI served as the starting point for many later European projects.

<sup>(158)</sup> <http://www.transplant-observatory.org/>



### Further information:

Website at DG Research and innovation:  
[http://ec.europa.eu/research/fp6/ssp/dopki\\_en.htm](http://ec.europa.eu/research/fp6/ssp/dopki_en.htm)

### Project team:

Project leader:  
 Organización Nacional de Trasplantes (ONT)  
 C/ Sinesio Delgado 6-8, Pabellón 3  
 28029 Madrid  
 SPAIN  
 Tel. +34 902300224  
 Fax +34 902300226  
 E-mail: [ont@mssi.es](mailto:ont@mssi.es)  
 Website: <http://www.ont.es>

### Associated partners:

- Agence de la Biomédecine, France
- Deutsche Stiftung Organtransplantation, Germany
- Hungarotransplant Public Service Cooperation, Hungary
- Centro Nazionale Trapianti, Italy
- Organização Portuguesa de Transplantação, Portugal
- UK Transplant, United Kingdom
- Eurotransplant International Foundation, based in the Netherlands, covering several European countries
- Swisstransplant, Switzerland
- Transplant Coordinating Centre of the Czech Republic, Czech Republic
- Slovenija Transplant, Slovenia
- Ministry of Health And Social Welfare, Croatia

### EU contribution

This project has received co-funding from the European Union in the framework of the **6<sup>th</sup> Research Framework Programme** (Research priority: 2.2. Public health issues, including epidemiology contributing to disease prevention and responses to emerging rare and communicable diseases, allergies, procedures for secure blood and organ donations, non-animal test methods).

# European Group for Coordination of National Research Programmes on Organ Donation and Transplantation (ALLIANCE-O)

*Project reference: This project has received co-funding from the European Union in the framework of the 6<sup>th</sup> Research Framework Programme (CA-011853-ALLIANCE-O).*

ALLIANCE-O, the European Group for Coordination of Research Programmes on Organ Donation and Transplantation was a Coordination Action (2004–2007) funded under the ERA-NET scheme of the Sixth Framework Programme<sup>(159)</sup>. ALLIANCE-O was one of the first collaborations between national transplantation agencies in the organ transplantation field funded by the European Commission.

Coordinated by the Agence de la Biomédecine in France, ALLIANCE-O has brought together representatives of national public transplant organisations from seven countries: France, Germany, Hungary, Italy, Portugal, Spain and the United Kingdom.

The main objective of ALLIANCE-O was to set up a coordinated network of organ donation and transplantation. Further, the project aimed to identify existing programmes and to propose common strategies and joint initiatives for better coordination and efficiency of organ transplant systems in EU Member States.

## ALLIANCE-O activities and results

The project has organised its activities along six technical work packages that took into account the following aspects of organ transplantation:

- expanding the donor pool,
- allocation rules and their impact on equity and efficiency,
- increasing safety and quality of organ transplantation,



Project summary at [http://ec.europa.eu/research/fp7/pdf/era-net/fact\\_sheets/fp6/alliance-o\\_en.pdf](http://ec.europa.eu/research/fp7/pdf/era-net/fact_sheets/fp6/alliance-o_en.pdf)

- evaluation methods of transplantation performance,
- fundamental research activities,
- ethical and legal aspects.

Along these aspects, the ALLIANCE-O project has managed to review and compare the then existing national/regional transplantation programmes, their processes and outcomes. Based on the benchmarking analysis performed by the

<sup>(159)</sup> The objective of the ERA-NET scheme (ERA: European Research Area) is to step up the cooperation and coordination of research activities carried out at national or regional level in the Member States and associated states through: the networking of research activities conducted at national or regional level, and the mutual opening of national and regional research programmes.

project, state-of-the-art overviews were produced and recommendations were drawn up and piloted in selected fields.

### The analysis regarding the possible expansion of the donor pool involved harmonised data collection for 39 countries with respect to the year 2004

The results of this analysis pointed out important variations in many aspects of the donation and transplantation activity, notably in living donation activities, non-heart beating donation and the size of waiting lists, as well as mortality while on waiting lists. To understand these differences in donation and transplantation activities and outcomes, the project analysed and compared the basic national characteristics and frameworks such as socio-demographic, economic, healthcare factors and mortality levels for every European country. The results suggested that factors of mainly organisational and structural nature may explain many of the differences between the countries.

“Additionally, the ALLIANCE-O project provided paramount information including on legal and ethical aspects that was available to policy-makers and experts involved in the preparation of the organ Directive. It can be considered as a strong basis that particularly inspired and allowed to build-up further EU projects and Joints Actions in the field.”

Agence de la Biomédecine, France

The project also analysed existing programmes that aimed at **expanding organ donation and retrieval in ALLIANCE-O countries**. The project found common approaches to increase the donor pool, but also substantial differences with regards to the legal, technical, organisational, training, educational, promotional and financial initiatives and human resources. Overall, the project has established that while organisational differences were relatively small, in terms of technical aspects important differences existed, especially with regard to the use of expanded criteria donors and special techniques.

Based on the findings of the state-of-the-art and benchmarking analysis, the ALLIANCE-O group developed a set of statements and recommendations about different aspects of expanding the donor pool such as brain death donors, non-heart beating donors, living donation, promotion of organ donation and transplantation. Further, the ALLIANCE-O made recommendations about common methods for donor pool estimation. A set of indicators to estimate the donation potential and to evaluate the outcome of the donation process and the system's global effectiveness have been proposed by the ALLIANCE-O group.

The project has also reviewed and evaluated **organ allocation rules** and practices in the participating countries and their impact on equity and efficacy. The state-of-the-art analysis of current organ allocation activities pointed out that a wide range of allocation systems, procedures, protocols and allocation criteria existed in the countries. ALLIANCE-O prepared a set of statements and proposed general recommendations for best practices in organ allocation. It also made the ground for developing a common simulation tool. Such activity included the analysis of allocation systems and building on the experiences of an experimental pilot study performed among selected partners using the organ allocation simulation prototype that was developed by the project coordinator. Based on these activities, ALLIANCE-O managed to build a conceptual toolbox for health policymakers and institutions involved in organ allocation in Europe and proposed a common simulation tool for allocation policies.

### The ALLIANCE-O project was also able to collect and analyse the then existing safety and quality aspects of donation and transplantation systems in the countries of consortium members

An inventory and comparison of existing safety and quality procedures were prepared. In terms of safety practices, the overview focused on transmittable diseases and the relevant tests thereof. While with the quality systems, the project, in addition to the existence of such systems, focused on the approach applied to the donation and transplantation process. The project has managed to elaborate safety recommendations and recommendations to increase quality. It also developed '**common best practices for a quality management system in the transplantation process**' (ALLIANCE-O White Paper). In relation to safety and quality issues, the group worked

out the first draft of a single European donation form that would include the same data set all over Europe to give impetus to future collaboration in harmonisation efforts.

The ALLIANCE-O work on **evaluation of transplantation performance** involved a state-of-the-art review of transplant methods and a summary of findings related to a wide range of issues of performance measurement such as data collection process, funding arrangements for data collection, statistical analysis and audit, software used in data analysis and how statistical results are made available to the public. By providing a summary of methods that have proved to be helpful in the analysis of transplant data in Europe, it served as a guide to units who were about to set up methods for monitoring and analysis transplant outcomes. Further, the project was able to draw a proposal for standardised methods to monitor the performance of different transplantation teams and standardised risk factors.

### The ALLIANCE-O project has managed to build an inventory of the then existing research projects/programmes in the domain of organ transplantation

The overview identified the main focuses and needs in basic research and presented possible

strategies to enhance the performance of research and avoid duplications. Based on this overview, the project developed recommendations on key functions, tasks and responsibilities of a national body dedicated to research in the field of donation, procurement and transplantation.

Furthermore, **legal and ethical aspects of organ donation and transplantation** were identified and analysed by the project. Based on the findings, the ALLIANCE-O elaborated general recommendations to help focus the then upcoming EU legislation on deceased organ donation and on living donation.

ALLIANCE-O organised a final workshop on 24 October 2007 to disseminate its main results to a European audience of representatives from competent authorities and from research bodies, transplant professionals and journalists. The summary of the project's main activities and results were published among other communications in the ALLIANCE-O White Paper ([www.agence-biomedecine.fr](http://www.agence-biomedecine.fr)).

### ALLIANCE-O outcomes

The project highlighted areas of improvement in organ donation and transplantation, set the needs and encouraged Member States to

	Eurotransplant (1)	France	Italy	Spain	Scandia (2) Transplant	UK (3)	ROI (3)
Cadaveric donors	1850	1119	1042	1443	361	710	80
pmp	15.5	18.3	18.5	33.8	15	12.1	21
Cadaveric kidney transplants	3345	1991	1489	1991	654	1297	133
pmp	28.1	32.5	26.4	46.7	27.2	22	35
Living donor kidney transplants	646	136	135	60	271	439	0
pmp	5.4	2.2	2.4	1.4	11.3	7.4	0
Liver transplants	1391	833	867	1037	248	633	32
pmp	11.7	13.6	15.4	24.3	10.3	10.7	8.4
Heart + heart/lung transplants	590	299	317	290	134	164	15
pmp	5	4.9	5.6	6.8	5.6	2.8	3.9
Lung transplants	405	92	65	145	103	135	0
pmp	3.4	1.5	1.2	3.4	4.3	2.3	0

(1) Eurotransplant includes Germany, Austria, Belgium, Luxembourg, The Netherlands and Slovenia  
 (2) Scandia Transplant includes Denmark, Norway, Finland and Sweden  
 (3) Figures taken from National Transplant Database, March 2004. All others are provisional figures from Organización Nacional de Trasplantes (ONT)  
 Note: definition of a cadaveric solid organ donor varies between countries.

Organ donation rates in 2003, when the project was initiated

([http://ec.europa.eu/research/fp7/pdf/era-net/fact\\_sheets/fp6/alliance-o\\_en.pdf](http://ec.europa.eu/research/fp7/pdf/era-net/fact_sheets/fp6/alliance-o_en.pdf))

Making systems compatible: in 2004 several countries had launched national research programmes to look into ways to help organ supply meet demand. Projects tended to focus on how to expand the donor pool, improve organ allocation, ensure the safety and quality of transplants, and evaluate and disseminate results. Yet there was little coordination between the different national research programmes in Member States. One of the main barriers to joint activity was the variation in organisational structures. Some countries had a national transplantation agency, under the control of the Ministry of Health, while others had appointed an independent foundation. Several countries had joined together to create a supranational organisation, such as Eurotransplant and Scandiatransplant — but many Member States had no central body at all.

Despite their differences, the organ transplant community in Europe recognised the need for greater transnational coordination of research programmes to expand the overall donor pool within the EU, to provide a transparent allocation system and enable the movement of organs and/or patients across borders in order to minimise shortages and avoid the waste of any transplant material.

The European Group for Coordination of Research Programmes on Organ Donation and Transplantation (ALLIANCE-O) had been established to bring together representatives from the organisational bodies of seven Member States, and coordinated by the Etablissement Français des Greffes — an institution now replaced by the Agence de la Biomédecine.

[http://ec.europa.eu/research/fp7/pdf/era-net/fact\\_sheets/fp6/alliance-o\\_en.pdf](http://ec.europa.eu/research/fp7/pdf/era-net/fact_sheets/fp6/alliance-o_en.pdf)

develop shared structures, definition and methods as well as common frameworks for data collection, training and evaluation.

Based on the overview of different aspects of organ transplantation, the project was able to point out — as a result — important variations in most of the aspects of post-mortem donation, living donation, allocation programmes, safety and quality criteria, and describe the transplant organisation system at national/regional/local levels of the seven participating Member States. Based on this global state-of-the-art analysis, a conceptual toolbox for organ allocation was generated. This led to the first outline of the EU donation form and made medical and organisational information available to countries and transplant agencies initiating transplant programmes or developing their system.

### ALLIANCE-O fostered networking

The Alliance Consortium also recommended better interaction between all professionals of the field and called for a better sharing of tools and expertise.

As set out in the ALLIANCE-O conclusions in the project's White Paper: 'Many of the proposals imply collaboration between countries. The goal is to establish more powerful strategies but not to reach a unique uniform system:

- common definition of terms is mandatory to share experience and results,
- common approach in tools used for organisation, training, education, allocation, safety, quality and evaluation, could avoid duplication of work and save time.'

In doing so, ALLIANCE-O facilitated the expansion and reinforcement of the network of transplant agencies.



### Further information:

Project website

[http://ec.europa.eu/research/fp7/pdf/era-net/fact\\_sheets/fp6/alliance-o\\_en.pdf](http://ec.europa.eu/research/fp7/pdf/era-net/fact_sheets/fp6/alliance-o_en.pdf)

More information and communication on the project

[www.agence-biomedecine.fr](http://www.agence-biomedecine.fr)

<http://www.agence-biomedecine.fr/IMG/pdf/dp-allianceo.pdf>

### Project team:

Coordinator:

Agence de la Biomédecine

1 avenue du stade de France

93212 Saint-Denis La Plaine Cedex

FRANCE

Fax +33 155936550

Contact: <http://www.agence-biomedecine.fr/Contact-us>

Website: <http://www.agence-biomedecine.fr/About-us>

### Partners:

- Ministry of Health, Deutsche Stiftung Organtransplantation, Germany
- Ministry of Health, Hungarotransplant Psc., Hungary
- Istituto Superior di Sanità, National Transplant Centre, Italy
- Ministry of Health, Organizaçao Portuguesa de Transplantaçao, Portugal
- Centro Nacional de Trasplantes y Medicina Regenerativa, Spain
- Ministry of Health, United Kingdom Transplant, United Kingdom

### EU contribution

Project reference: This project has received co-funding from the European Union in the framework of the **6th Research Framework Programme** (CA-011853-ALLIANCE-O)

## European Training Programme on Organ Donation (ETPOD)

*This project has received co-funding from the European Union in the framework of the Public Health Programme 2003–2008 (Grant: 2005205).*

Different levels of professional staff are involved in the process of organ donation and transplantation, such as: (1) healthcare professionals in targeted donor units such as intensive care, recovery and emergency room departments; (2) healthcare professionals in charge of organising the generation of donors or those due to join a Transplant Coordination Office (TCO) and key donation professionals (KDP) wishing to update their knowledge and reinforce their competences; (3) donor programme managers responsible for national, regional, local and/ or hospital organisations with high activity in organ procurement and transplantation.

Increasing organ donation rates to its maximum potential requires that all those levels of professional staff have a comprehensive knowledge and reliable information available on most aspects of organisation and procedures of organ donation and transplantation. The project 'European Training Programme on Organ Donation' (ETPOD) aimed at disseminating such knowledge by means of a multi-module training programme.

The project started in January 2007 for 3 years and involved 20 organisations from 17 countries. Through its activities the project reached 25 target areas (TA's) of organ donation and

transplantation. ETPOD was coordinated by the University Hospital of Barcelona and its Centre for Transfer of Knowledge, Technology and Innovation (TPM).

### ETPOD developed four training modules for the various levels of professionals involved in organ donation

ETPOD started with a comparative analysis to assess organ donation rates before and after the implementation of the ETPOD training programmes as well as a study of the training needs of the various levels of healthcare professionals involved in the process of organ donation, in accordance with the organisation structure and resources of each TA. The ETPOD training programme was developed and implemented in four course modules, addressing the various professional levels.

- (1) A Training for Trainers Programme aimed to train Key Donation Professionals (KDPs) as multipliers of training actions, providing them with skills required so that they could replicate the training programme within the target areas (TAs) in an accurate manner so as to successfully carry out the 'Essentials in Organ Donation Training'.
- (2) An Essentials in Organ Donation Training aimed at providing fundamental training related to the donation-procurement process, in order to promote among healthcare professionals the active detection of possible donors and to obtain their cooperation.
- (3) The Professional Training on Organ Donation Programme aimed at training healthcare professionals in charge of organising the generation of donors and/or those due to join a Transplant Coordination Office as well as Key Donation Professionals wishing to update their knowledge and reinforce their competences.
- (4) The Organ Donation Quality Managers Training aimed to provide participants with the theoretical, technical and practical know-how required to efficiently organise



ETPOD website

and manage a transplant procurement office concerning the quality indicators of the organ donation process success. This programme is addressed to responsible of national, regional, local and hospital organisations with high activity in organ procurement and transplantation.

### Within this framework, the learning methodology to implement the ETPOD was based on two modalities: blended learning and face-to-face training

The methodology of the project followed the cycle of: (1) analysis of the country's current situation, (2) designing an adapted training programme to the needs, (3) validation and implementation of the programme, (4) follow-up, (5) evaluation and, finally, (6) analysis its transferability observing again the country's current situation. The strategy was based on the awareness that each participant country has different donation rates per million inhabitants (pmp); therefore the project included the following actions:

- transfer of the gained expertise between countries with higher organisational development and those with less organisational development in the respective processes by training programmes with international faculty staff from different partner countries;
- development of a European training programme on organ donation addressed to different professionals' profiles involved in the donation process at national, regional, local and hospital levels;
- design and adaptation of specific contents to be developed in accordance with the analysis of educational needs previously identified in each target area (TA).

Within this framework, the learning methodology to implement the ETPOD was based on two modalities: blended learning and face-to-face training. Learning occurs when a series of processes takes place ending with the new knowledge assimilation and objectives accomplishment. The ETPOD trainings used a training approach called experience-based learning action, that the Institute for LifeLong Learning (IL3) has successfully used in similar trainings before. It allows participants to acquire up-to-date focused knowledge, to develop the know-how into professional competences and skills,

to develop the performance of good practices by 'show-how', and to finally enable them to apply the newly acquired knowledge and experience adapted to their own reality.

The execution of the project was carried out through four working groups (WGs) involving 17 countries and 20 partner organisation representatives.

WG1 — **Database Source Group** was responsible for obtaining information on the target areas before and after the implementation of the ETPOD courses in order to evaluate their influence on the organ donation rates and the staff training requirements.

WG2 — **Basic Training Group** coordinated and followed up the Training For Trainers and Essentials in Organ Donation Training Programmes.

WG3 — **Professional Training Group** coordinated and followed up the Professional Training on Organ Donation Programme plus the E-learning Virtual Modules.

WG4 — **Managers Training Group** coordinated and followed up the Managers Training On Organ Donation.

### Basic Training Group to prepare Senior Transplant Coordinators

The Training for Trainers programme allows preparing Senior Transplant Coordinators to



CD-ROM for dissemination of ETPOD results

implement in their own Target Area the Essentials in Organ Donation Training. The Training for Trainers programme is based on the blended learning methodology, which considers both the online and the face-to-face training. Courses were designed, developed and implemented in English.

The Essentials in Organ Donation Training is the basis of WG2. Its aim is to provide training related to the donation-transplant process, in order to provide healthcare professionals with the knowledge and skills needed to be in charge of an organ donation-procurement programme in a competent and successful way.

### Professional Training Group for Junior Transplant Coordinator with experience of up to 2 years

The aim of the Professional Training on Organ Donation Programme is to train Transplant Coordinators in charge of organising the generation of donors. The participant's profile of this programme is that of a Junior Transplant Coordinator (experience up to 2 years) or with an interest in transplant coordination with possibilities to be a future Transplant Coordinator. Communication and computer skills are essential.

The Professional Training on Organ Donation programme is based on the blended learning,

which considers both the online and the face-to-face training. Courses are designed, developed and implemented in English language and consist of modules such as: Donor Management and Organ Viability e-learning module; Organ Retrieval, Preservation and Distribution e-learning module; and the Professional Training on Organ Donation face-to-face programme.

### Managers Training Group for organising, managing and evaluating a transplant area

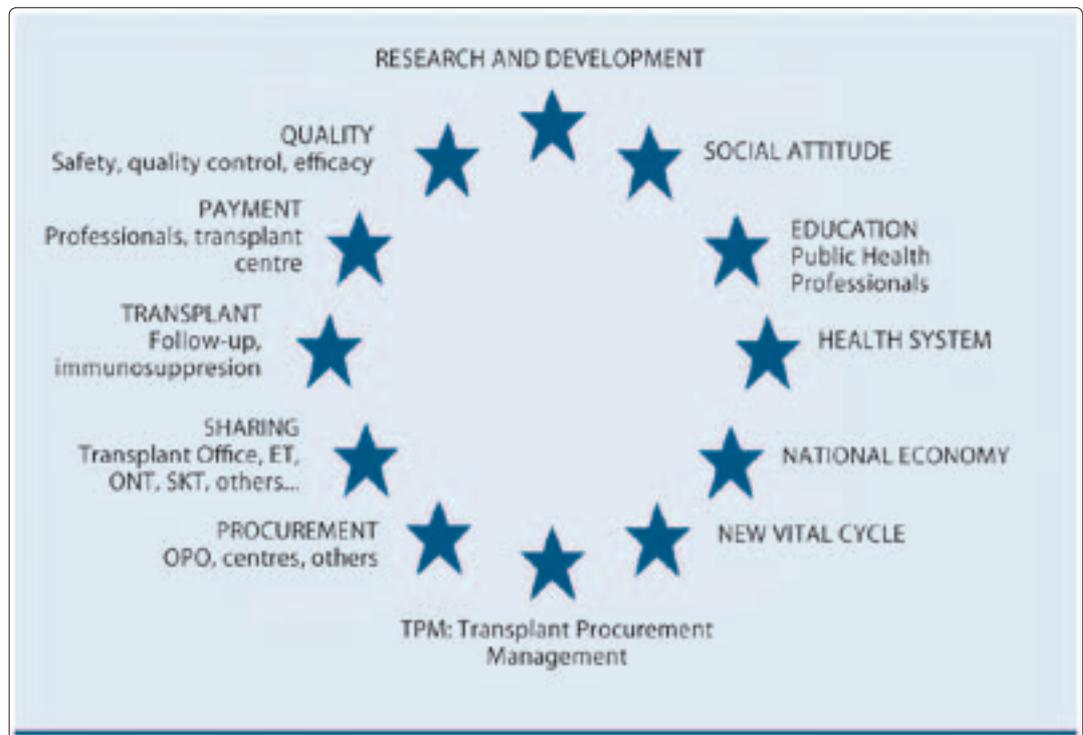
The aim of the Organ Donation Quality Managers Training is to provide the skills required for organising, managing and evaluating a transplant area and promote the implementation and evaluation of quality and safety measures to hospital, regional or national donation office responsible included in the Target Areas.

### ETPOD project achievements

The collaborative partnership and networking has been accomplished by means of the ETPOD Partners Community hosted on the website <http://etpod.il3.ub.edu/>. In addition, participants built a professional relationship during the online modules and had the opportunity to meet in person during the face-to-face courses. This allowed them to create a solid networking that has gone further than the scope of ETPOD.



*The new vital cycle: Donation and transplantation process (transplant procurement management: transplant coordination organisation model for the generation of donors)*



*Stars of the donation-transplantation process (transplant procurement management: transplant coordination organisation model for the generation of donors)*

A survey was carried out in the 25 target areas in order to determine the training needs concerning the whole process of the organ donation according to each level. The courses were developed in accordance with the results.

All the planned courses have been created and implemented at the three different training levels. Furthermore, all the courses were evaluated by the participants after their implementation. The average score was 4.35 on a 1–5 scale.

To reach a relevant number of direct beneficiaries, each target area responsible person selected the five candidates to be directly trained within ETPOD. Moreover, the EOD seminars trained around 120 participants in each target area. Fifty-one participants attended the Training for Trainers (both online and face-to-face training) of which 49 participants attended the Professional Training on Organ Donation (both online and face-to-face training); 23 participants attended the Organ Donation Quality Managers (face-to-face training).

As the conducted surveys indicated, the procured brain death donors in the 25 target areas showed a rise of 27.8 % ( $p=0.01$ ). The ETPOD Project has further been presented in several scientific forums.

ETPOD has created quality educational materials that count with the support of the participating organisations. The EOD seminars are being carried out in several TA and non-partner countries which have shown interest in the developed training courses. Moreover, the European Commission mentioned ETPOD in the Action plan on Organ Donation and Transplantation (2009–2015).

The ETPOD Project built a public access website in order to provide information about the project and also about the results. It is available at <http://etpod.il3.ub.edu/>. In order to keep track of all the different outputs of the project, the ETPOD team has created a web application to compile all the information that is available at <http://www.etpod-dissemination.eu> upon registration. The project deliverables can also be accessed through the project database of EAHC (see Infobox).

*“Altogether, 3 163 participants attended the EOD seminars in the 25 target areas.”*



### Further information:

EAHC Project Database:

<http://ec.europa.eu/eahc/projects/database.html?prjno=2005205>

Project website

<http://etpod.il3.ub.edu/>

Dissemination page:

<http://www.etpod-dissemination.eu>

### Project team:

Fundació Bosch i Gimpera

Ciutat de Granada 131

08018 Barcelona

SPAIN

Tel. +34 935677410

Fax +34 934279798

### Associated partners:

- Institutul Roman de Training (NAT), Romania
- Universitat de Barcelona Virtual (UBV), Spain
- Organización Nacional de Trasplantes (ONT), Spain
- Medicinische Universität Wien (UHV), Austria
- Agence de la Biomedicine (ABM), France
- Deutsche Stiftung Organtransplantation (DSO), Germany
- Istituto Superiore di Sanità (ISS), Italy
- Fondazione per l'Incremento dei Trapianti d'Organo (FITO), Italy
- Hungarotransplant Egészségügyi Koordináló Társaság (Hungarotransplant), Hungary
- Nacionalinis Organu Transplantacijos Biuras (NBOT), Lithuania
- Organização Portuguesa de Transplantação (OPT), Portugal
- Dolnoslaska Fundacja Transplantacji (LSF), Poland
- Akademi Medycznej w Warszawie (MUW), Poland
- Centrum Organizacyjno Koordynacyjne Transplantacji, Poland
- Paraskevidion Surgical and Transplant Centre (PSTC), Cyprus
- Hellenic National Transplant Organisation, Hellenic Department of Health (EOM), Greece
- Martinska Fakultna Nemocnica (UHM), Slovakia
- Zavod Republike Slovenije za Presaditve Organov in Tkiv Slovenija Transplant, Slovenia
- Akdeniz Universitesi Organ Nakli Egitim, Arastirma ve Uygulama Merkezi (AUTC), Turkey
- Executive agency for Transplantation Bultransplant (EAT), Bulgaria
- Skane Lands Landsting, County Council of Skane, Sweden
- Sihtasutus Tartu Ulikooli Kiilikim (TUC), Estonia

### EU contribution

This project has received co-funding from the European Union in the framework of the **Public Health Programme 2003–2008** (Grant: 2005205).

## European Living Donation and Public Health (EULID)

*This project has received co-funding from the European Union in the framework of the Public Health Programme 2003–2008 (Grant: 2006211).*

Live donation has been growing in recent years due to the advances in the field of organ transplantation and its success as a treatment to procure quality-adjusted life years for many patients with end-stage diseases. The choice of transplantation from a living donors' offers some advantages compared to that from a deceased donor. However, it also carries disadvantages related to the donors' risks in terms of health and safety. Several controversial ethical aspects are also to be considered.

### There is a great heterogeneity among European countries' legislations, ethical concerns, protection systems and donor's data registries on the topic

In Directive 2004/23/EC of the European Parliament and of the Council it was recognised that *'... it is necessary to increase confidence among the Members States in the quality and safety of donated tissues and cells, in the health protection of living donors and respect for deceased donors and in the safety of the application process...'*

Additionally, the Action Plan on Organ Donation and Transplantation (2009–2015): Strengthened Cooperation between Member States encourages Member States to promote the exchange of best practices on living donation programmes (Priority Action 3). Furthermore, the Commission states that it *'... will help to develop adequate tools to facilitate the proper collection of information on the medical, psychological, financial and social consequences of a living donation — in the short and the long term. This information, coupled with the exchange of best practices on living donation programmes among the Member States, should help to develop evidence-based guidelines and consensus documents, and address the selection, evaluation and follow-up of the living donor.'*

The main objective of the project European Living Donation and Public Health (EULID) was to analyse the European situation regarding legal, ethical, protection and registration practices related to living organ donation, in order to set

standards and recommendations that guarantee the living donor health and safety.

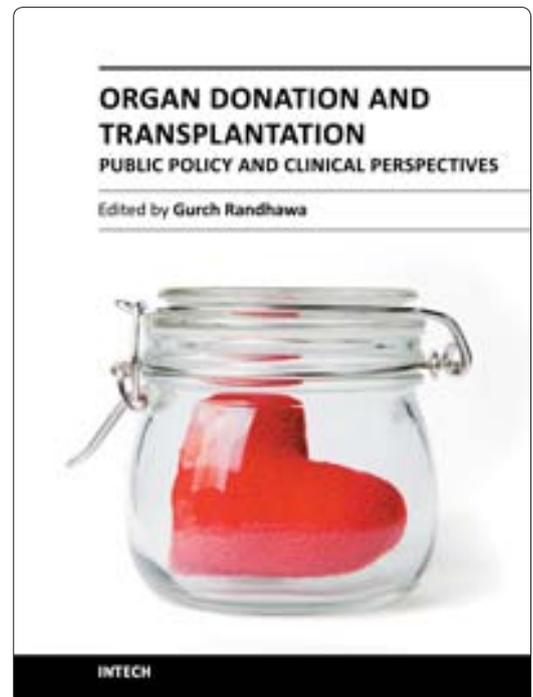
Twelve partners from 11 countries worked for 30 months (May 2007 to October 2009) to reach a consensus on the main requirements for the protection of living donors by focusing on the different issues related to the main objective of the project. The project was coordinated by Hospital Clínic of Barcelona (Spain).

### Legislation and ethical concerns regarding living donation

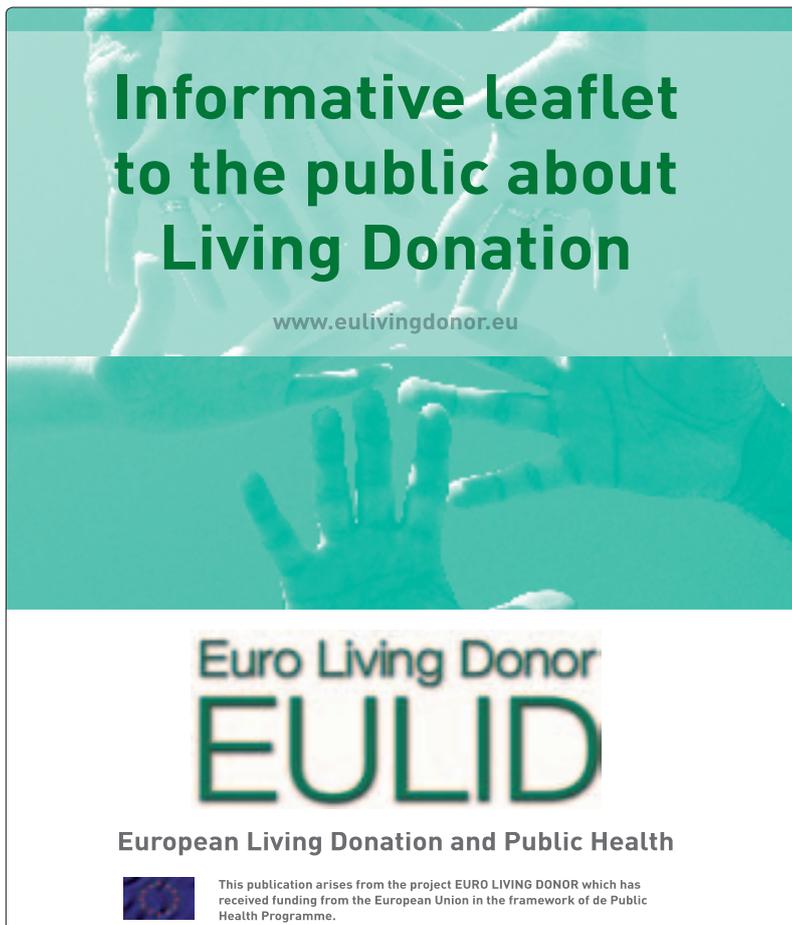
The work package on legislation and ethical concerns regarding living donation analysed and compared the different European countries' legal and ethical frameworks on living donor's health and safety in order to establish European legal and ethical recommendations.

The partners have collaborated through answering the survey with data related to their own country and discussed and reached consensus about ethical concerns regarding living donation. The following reports have been drafted: (1) Report on ethical concerns; (2) Report on current legislation practices; and (3) Recommendations report of standard procedures on living donor donations.

Great heterogeneity between partner countries' legislations regarding living donation has been encountered.



*Organ Donation and Transplantation — Public Policy and Clinical Perspectives, Edited by Gurch Randhawa, ISBN 978-953-51-0039-3, Hard cover, 284 pages, Publisher: InTech, Published: 8 February, 2012 under CC BY 3.0 license, in subject Medicine, doi:10.5772/1486*



*EULID leaflet for dissemination*

### Protection of the living donor in European countries

The work package on protection of the living donor in European countries determined the potential risks for the living donor and analysed whether there are specific legislative or non-legislative systems or practices for living donor's protection. The work package developed and wrote an informative leaflet directed to the general public and conducted a survey on living donor's satisfaction in the project partners' European countries. The following reports have been produced: (1) Report on risks for living donors; (2) Current protection practices and final recommendations for the protection of living donors; (3) Informative leaflet translated into all partners' languages; (4) Guidelines: What information an informative leaflet for living donors should contain; (5) Report on living donor's satisfaction survey results.

### E-registry database model on living organ-donors' data

This Registry work package established and validated an e-registry database model on

living organ-donors' data that allows having a common European database registry and common national registries on the issue. The partners contributed the list of hospitals with living donor activity, tested the online database model and entered living donor cases in the database. The following reports have been produced under the umbrella of this work package: (1) List of hospitals with a living donor programme; (2) Report on current registration practices; (3) Report on the recommended data to be collected about living donors; (4) Report on the implementation and use of the e-registry model; and (4) Recommended strategy to monitor living donors.

Laws and some institutions' rules on data protection limit the availability of all donors' data. The online registry, once created, required a long period of testing before the partners could start entering real cases. Therefore, three levels of data to be registered were created: basic, recommended and excellence data. The database design furthermore recognises the need for data protection: access to the database requires specific-person authorisation and a password is needed to log in. Furthermore, the data collected makes impossible the identification of donors, since no personal data is collected. Finally real cases were entered, with more than 700 donors registered.

### Minimum set of final recommendations

The project's final recommendations were elaborated with a consensus among project partners, even though there is a great heterogeneity among the different countries on the different issues discussed. At the same time, this heterogeneity leads to an agreement on the minimum recommendations necessary to guarantee living donors' health and safety. The final minimum set of recommendations are as follows.

With respect to legislation:

- prohibition and penalisation of organ trafficking, transplant tourism and commercialism, including incentives;
- prohibition of minors and persons unable to give consent;
- authorisation of transplant centres and registry of living donors under the control of authorities;
- regulation of independent commissions (evaluation, information, approval);

- reimbursement of expenses related to donations and provisions to protect donors and their families from discrimination, permanent injury or death.

#### With respect to ethical aspects:

- the altruism of living donors should be object of the most elevated consideration by the community;
- the promotion of living donation should not impede cadaveric donation and its development to its maximal potential;
- organ trafficking, commercialism or incentives are ethically unacceptable and should be banned;
- living donor candidates should be protected from any form of physical, psychological, social or economic disadvantage;
- the autonomy of potential living donors should be respected if there is not a greater risk;
- the reimbursement model should be implemented by health authorities to protect donors;

#### With respect to the protection of living donors:

- careful selection of information to the living donor is crucial for donor safety; not everyone who wants can become a donor;
- sick leave with 100 % payment and socio-medical and protective support if sick leave is prolonged;
- full economic reimbursement during investigation and procedure;
- financial coverage in case of unforeseen events related with the procedure;
- medical follow-up obligated and psychosocial support if needed;
- living donation should not be a limitation for getting a life insurance, mortgage or any other social assistance or benefit;
- homogenous protection systems within the European Union with a defined minimum standard.

#### With respect to registration practices:



*EU living donor CD-ROM for dissemination of results  
(available at <http://www.eulivingdonor.eu/eulid/results.html>)*

- registration of all living donors is obligated for the purpose of traceability, safety and transparency of activity and procedure outcome;
- collection of living donor data has to be done through an established central database system, accessible by appropriately authorised persons;
- data on identification, country of residency, nationality, type of donation, healthcare institutions and outcome must be registered, with protection of the donor's proper privacy; an official point of contact must be registered at the embassy of the donor's country of residence;
- a regulatory audit is mandatory and data should be both monitored on a national and institutional level.

The final complete set of results and outputs of EULID are disseminated on the EULID website (EULID CD) (<http://www.eulivingdonor.eu>) for the public and professionals. EULID has prepared an informative leaflet about living donation. The leaflet is addressed to the general public and is available in 12 different languages.

Project results have also been widely disseminated to the professional community at various international conferences, and presented in Competent Authority meetings to reach national level. Additionally, the **Living Donor**

**Registry** is available through the EULID website for professionals after registration.

Final results have also been published in different scientific journals (Manyalich, Ricart, Martínez et al. EULID Project: European Living Donation and Public Health. Transplantation Proceedings, 41,2021–2024 (2009)). The results of the EULID Project have also been included in a chapter entitled 'European Living Donation and Public Health (EULID Project)' in the book 'Organ Donation and transplantation — Public Policy and Clinical Perspectives' (ISBN 978-953-51-0039-3), edited by Gurch Randhawa.

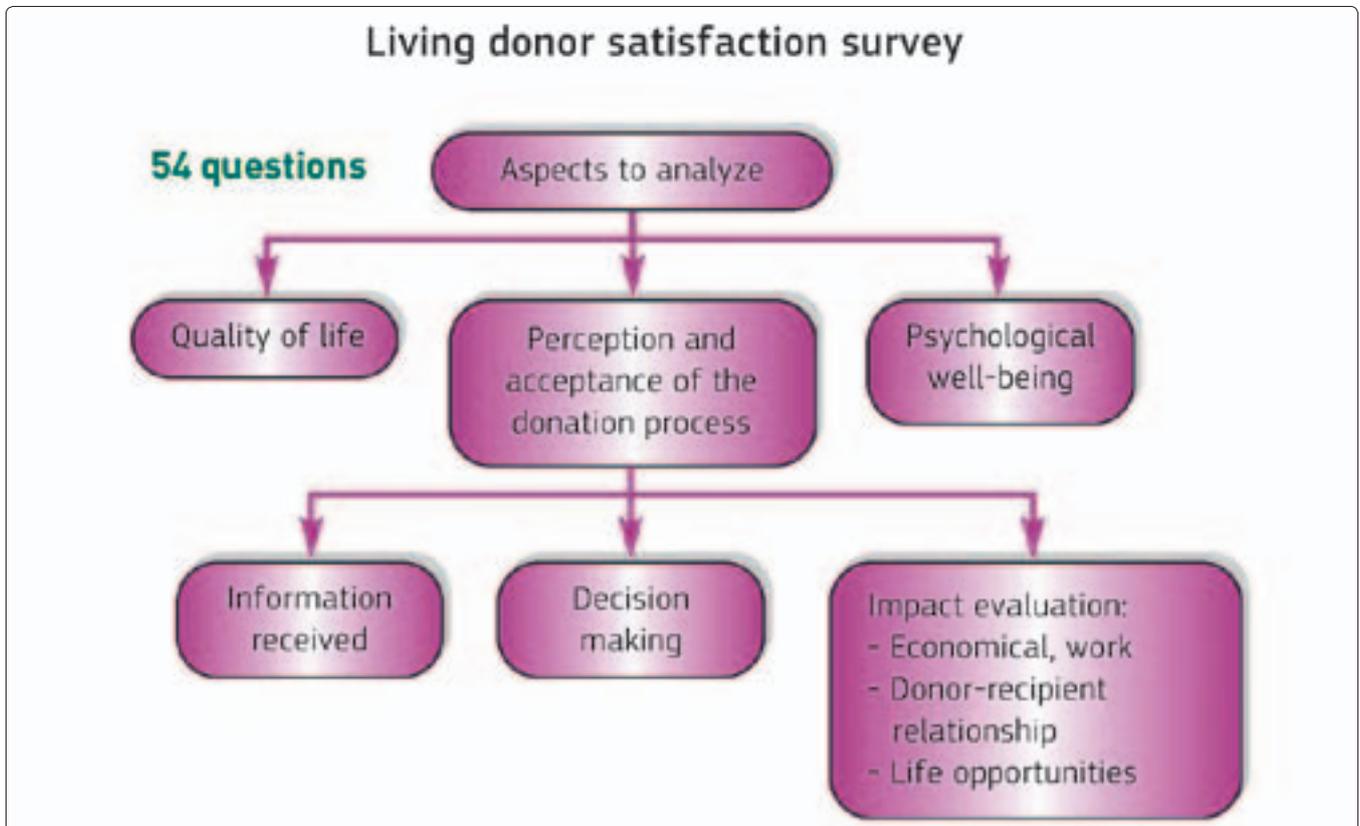
### Future perspectives

Among the tools developed, the EULID partners validated a living donor satisfaction survey that examines three spheres: information, perception and acceptance of the donation process; quality of life; and psychological well-being. Living donors' opinions through a satisfaction survey can be one of the tools to monitor the quality

and safety of the living donation programmes and the key to detect all the potential negative consequences of becoming an organ donor. With the idea of a Living Donor Observatory (LIDOB), researchers give continuity to these activities and at present the satisfaction survey is available online with more than 200 surveys collected through interviews from 11 countries and the data included in the database. The survey has been translated into 12 European languages.

Registry and follow-up are tools that allow benchmarks for quality control and implementation of improvement measures. Registry, when regulated, is one of the scarce tools that Member States have in order to detect unethical or forbidden practices, taking into account that, when obligated, the non-registration is by itself an infraction. It is necessary that registration models are developed by scientists themselves so that Member States have a reference to implement for the benefit of living donation health and safety.

The project ELIPSY and the Joint Action ACCORD take up these activities and bring them steps further.



Concept of the living donor satisfaction survey.

## Euro Living Donor EULID

### Further information:

EAHC Project Database:

<http://ec.europa.eu/eahc/projects/database.html?prjno=2006211>

Project website

<http://www.eulivingdonor.eu>

### Project team:

Hospital Clinic i Provincial Barcelona

C/ Villaroel, 170

08036 Barcelona

SPAIN

Tel. +34 932275400

Fax +34 934515272

### Associated partners:

- Paraskevaïdion Surgical and Transplant Centre of Cyprus, Cyprus
- Institute for transplantation of organs and tissues of the Republic of Slovenia, Slovenia
- Fundació Bosch i Gimpera, Spain
- Service de Transplantation Rénale Adulte, France
- Istituto Superiore di Sanita, Italy
- The University Hospital Rikshospitalet-Radiumhospitalet Trust, Norway
- Polish Transplant Coordinating Centre, Poland
- Hospital Geral Santo Antonio, Portugal
- National Agency for Transplantation, Romania
- Sahlgrenska University Hospital, Sweden
- NHS Blood and Transplant, United Kingdom

### EU contribution

This project has received co-funding from the European Union in the framework of the **Public Health Programme 2003–2008** (Grant: 2006211).

# European Framework for the Evaluation of Organ Transplants (EFRETOS)

*This project has received co-funding from the European Union in the framework of the Health Programme 2008–2013 (Grant: 20081101).*

In the Action Plan on Organ Donation and Transplantation (2009–2015): Strengthened Cooperation between Member States<sup>(160)</sup>, the Commission sets out, as one of the three main challenges in the field of organ transplantation, the importance of improving quality and safety of transplantation, among others through compiling the information concerning organ donations and transplantation in registers to facilitate the evaluation of post-transplantation results (Priority Action 9). As suggested by the Action Plan, this evaluation of post-transplant results would be facilitated through common definitions of terms and methodology and supported by compatible follow-up registers, or even EU-wide registers. Furthermore, the Action Plan recommends promoting common definitions of terms and methodology to help determine acceptable levels of risk in the use of expanded donors.

## Common definitions of terms and methodology for the future establishment of a European Registry of Registries on pre- and post-transplant outcome data

The **objective of the project** European Framework for the Evaluation of Organ Transplants (EFRETOS) was to provide such common

definitions of terms and methodology for the future establishment of a European Registry of Registries on pre- and post-transplant outcome data. The aim of such a European Registry of Registries is to be able to monitor patients and evaluate the results of transplantation, thereby to contribute to an improved effectiveness, quality and safety of organ transplantation.

In practical terms, *'the EFRETOS project was to describe the optimal content of a European Transplant Registry, based on the existing registries in Europe and current expertise. In addition, an appropriate functional framework, a feasible technical approach and the organisational prerequisites for realising a pan-European Registry had to be designed'*, states the project summary<sup>(161)</sup>.

The project EFRETOS was coordinated by the Eurotransplant International Foundation, a non-profit service organisation for allocation of donor organs, which is active for transplant centres and their associated tissue typing laboratories and donor hospitals in seven European countries. The work implemented during the EFRETOS project was based on the joint efforts of seven partner institutions and several collaborating organisations from 20 Member States of the European Union. The project was implemented in 2 years from May 2009 to May 2011.

EFRETOS was articulated around work packages focusing on different, but related issues such as common definitions, methodology, safety management and quality insurance.

## Development of a data dictionary

The aim of this work package was to develop a common data dictionary and definitions for all the variables that will be included in the registry. To be able to select and provide state-of-the-art definitions of the registry variables, three European expert groups were formed within the European Society for Organ Transplantation

What is the 5-year post-transplant survival rate for all patients treated in Europe with a renal allograft? How many patients were transplanted in Europe who suffered from the Hemolytic Uremic Syndrome? What donor and recipient factors influence the outcome after organ transplantation? Are there different strategies towards organ replacement therapies and related outcomes between the different countries in Europe? At present we cannot answer questions such as these, but a European Transplant Registry will enable us to do so.

[http://www.eurotransplant.org/cms/mediaobject.php?file=brochure\\_efretos\\_def.pdf](http://www.eurotransplant.org/cms/mediaobject.php?file=brochure_efretos_def.pdf)

<sup>(160)</sup> Communication from the Commission — Action Plan on Organ Donation and Transplantation (2009–2015): Strengthened Cooperation between Member States, <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:52008DC0819:EN:NOT>

<sup>(161)</sup> [http://www.eurotransplant.org/cms/mediaobject.php?file=brochure\\_efretos\\_def.pdf](http://www.eurotransplant.org/cms/mediaobject.php?file=brochure_efretos_def.pdf)

(ESOT) — EFRETOS partner — to overview the existing international data sets and collect all possible variables related to donors, recipients, organs and the donation and transplantation procedure.

Based on multiple expert reviews and discussions, a final set of variables has been agreed upon. The final set of variables and the data dictionary included the list of mandatory and optional variables per organ that are necessary to evaluate outcome and risk factors for quality and safety in deceased donation and organ transplantation and the respective definitions thereof.

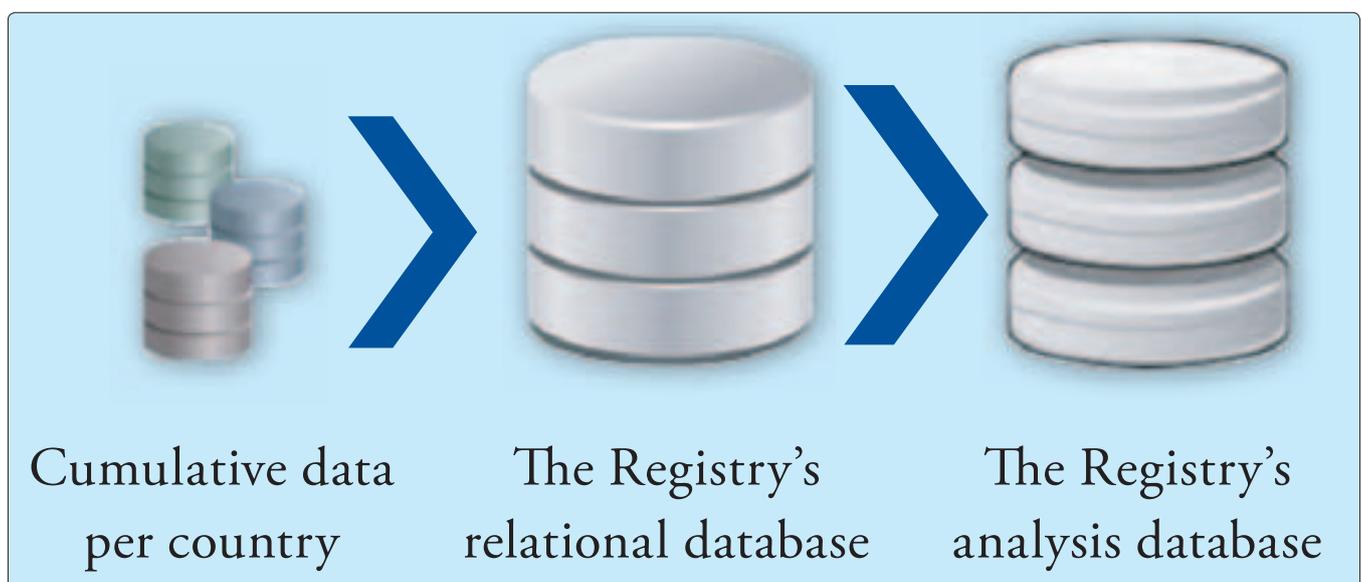
### Methods as well as legal and technical requirements

The aims of this work package were: (1) to develop data analysis methods for organ transplantation outcomes, and (2) to develop legal, functional and technical requirements for setting up and managing a future registry as well as to propose an organisation structure. The work in relation with these tasks mainly comprised an overview of existing statistical methods building also on previous project results on related topics and collecting the necessary system information via surveys to consortium members.

“The European Registry designed by the EFRETOS project is able to hold activity and outcome data on the transplantation of solid organs. The basic data set of the registry consists of all variables that are acknowledged to be of importance for a comprehensive evaluation of transplant outcomes.”

EFRETOS Report on the use of the European Registry of Registries, May 2011 <sup>(162)</sup>

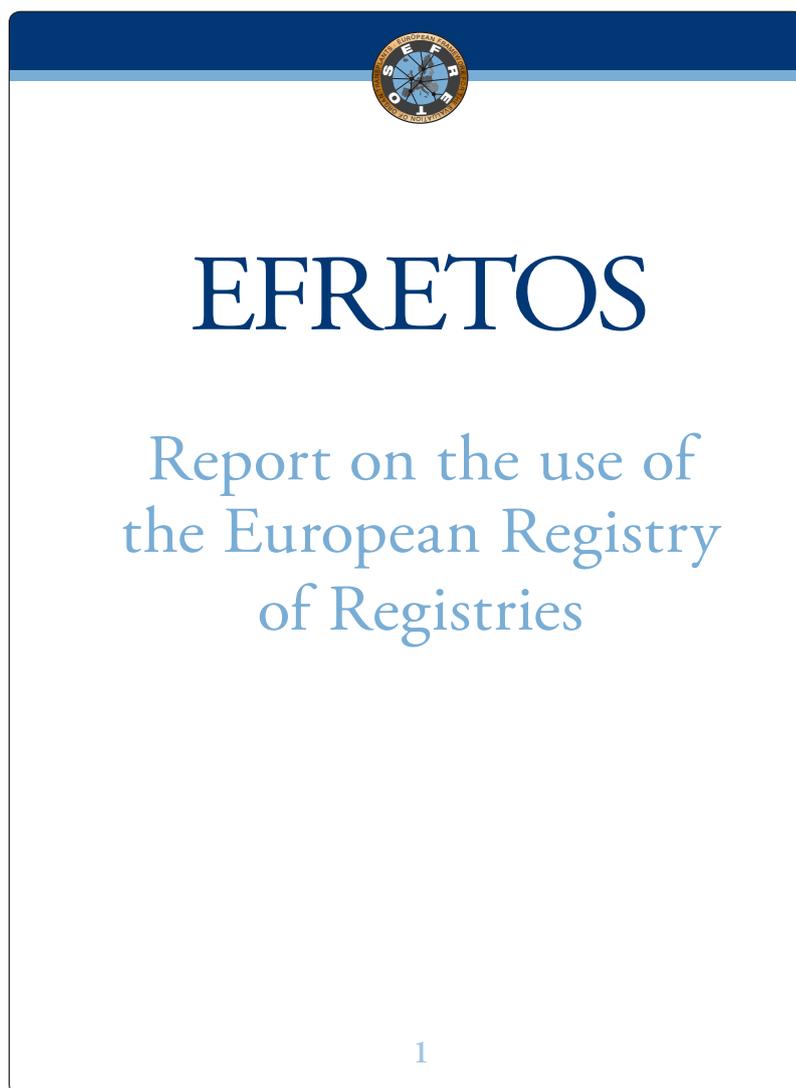
After developing the main features and elements, the EFRETOS project tested the technical feasibility of the proposed registry of registries. The purpose of the **pilot study** was to get an indication about how the different countries may be able to contribute to the European Registry, to identify possible problems and also provide evidence that such a pan-European registry can be created. The pilot study design focused on the evaluation of 1- and 5-year graft survival rates following kidney transplantation from deceased or live donation. Altogether five countries participated in the pilot, i.e. were able to provide national level data. The results of the pilot study provided further useful insights for the design of a European Registry and demonstrated its potentials.



Schematic overview of the European Registry

([http://www.eurotransplant.org/cms/mediaobject.php?file=brochure\\_efretos\\_def.pdf](http://www.eurotransplant.org/cms/mediaobject.php?file=brochure_efretos_def.pdf))

<sup>(162)</sup> ([http://www.efretos.org/images/EFRETOS\\_Deliverable %2011\\_FINAL.pdf](http://www.efretos.org/images/EFRETOS_Deliverable%2011_FINAL.pdf))



EFRETOS White Paper  
[http://www.eurotransplant.org/cms/mediaobject.php?file=EFRETOS-White\\_paper.pdf](http://www.eurotransplant.org/cms/mediaobject.php?file=EFRETOS-White_paper.pdf)

### Common safety management procedure in two specific areas

The objective of this work package was to develop a common safety management procedure in two specific areas: (1) the safety limits of the donation and transplantation process when non-standard-risk donors are considered for transplantation, and (2) the development of recommendations on how to build a European organ vigilance system. In order to make a state-of-the-art overview of the current practices, the work package designed and distributed a specific questionnaire among the EFRETOS consortium. Building on the survey results, the review of published literature and expert discussions, this work package developed recommendations on how to establish a comprehensive system that is also able to

adapt to national transplant systems for safety management and organ donation and transplantation. Furthermore, it provided recommendations on how to use non-standard-risk donors and the necessary data set to follow-up the recipients.

### Quality assurance system for obtaining high quality data on transplantation outcomes

The aim here was to set up a quality assurance system for obtaining high-quality data on transplantation outcomes. The project has overviewed the performance indicators used in existing registries, and gathered information from EFRETOS partners through a survey on presently adopted quality assurance systems. The results of this work led to a common shared methodology that enables the quality of post-transplant outcomes to be assessed and for these data sources and their handling to be validated.

### Main features and benefits of the Registry

The European Registry developed by EFRETOS is designed in a way to allow for a simplified reporting of such essential outcome data at national and European level that had not been available previously. *'The European Registry designed by the EFRETOS project is able to hold activity and outcome data on the transplantation of solid organs. The basic data set of the registry consists of all variables that are acknowledged to be of importance for a comprehensive evaluation of transplant outcomes'*<sup>(163)</sup>.

Furthermore, the EFRETOS project sees many advantages and benefits of having such a pan-European registry on transplantation. Among others, *'it will lead to the ability to investigate outcomes following transplantation for rare conditions, to explore outcomes following the transplantation from extended criteria donors, to identify factors associated with the occurrence of rare adverse events and to establish a European vigilance system'*, as pointed out in the report.

<sup>(163)</sup> EFRETOS Report on the use of the European Registry of Registries, May 2011, [http://www.efretos.org/images/EFRETOS\\_Deliverable\\_%2011\\_FINAL.pdf](http://www.efretos.org/images/EFRETOS_Deliverable_%2011_FINAL.pdf)

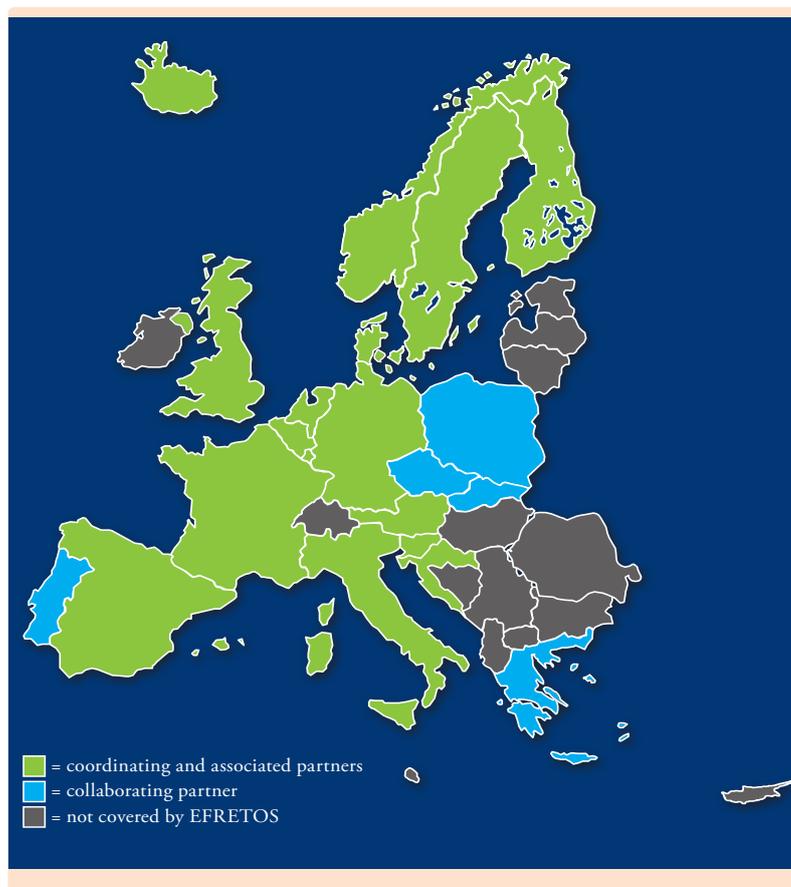
## Who can benefit from the European Registry and what has been done to reach them?

The main stakeholders and beneficiaries of the EFRETOS project are medical experts in the field of organ donation and transplantation, the European Commission and the national competent authorities in charge of organ donation and transplantation in the EU countries, and of course patients.

## The project had used various dissemination methods to reach its target groups

The **final results** of the EFRETOS project were summarised in the '**Report on the use of the European Registry of Registries**'. This comprehensive report gives a detailed description of the optimal content of a pan-European transplant registry, based on the existing registries and current expertise. Additionally, the report presents an appropriate functional framework, a feasible technical approach and the organisational prerequisites and key recommendations for its development and management.

A **final EFRETOS symposium** was organised in Brussels on 17 May 2011, entitled **Unifying Data Collection — Creating New Knowledge**, for a wide audience: scientists, researchers and medical professionals, politicians, policy-makers, patients and representatives of organisations in the field of organ transplantation. During the EFRETOS symposium, among other topics, the different stakeholders pointed out and discussed the main advantages of the Registry of Registries. The added value for European citizens of the Registry of Registries was emphasised as being the improved patient care and outcomes, improved information for patients and the public and increased transparency and accountability<sup>(164)</sup>. The main EFRETOS objectives and activities were first introduced in a layman brochure; regular updates on progress and results were disseminated via EFRETOS newsletters.



Countries covered by EFRETOS

## The final major recommendations for setting up a European Transplant Registry

The executive summary<sup>(165)</sup> outlines the 10 major recommendations from the EFRETOS project as following.

1. National or supranational registries on organ transplantation should be established in all countries. The structure of these registries should allow data delivery to the European Registry.
2. Besides collection of data on waiting list and transplant activities, data on the outcome of transplanted patients should be collected. National legislation ensuring that transplant programmes report on a mandatory and regular basis on the outcome of their patients would facilitate the data collection and reporting process.
3. The necessary funding for setting up and maintaining this national registry should be made available by the competent authorities.

<sup>(164)</sup> Report on the Symposium EFRETOS Unifying data collection, creating new knowledge. May 17, 2011, [www.eurotransplant.org/cms/index.php?page=efretos\\_report\\_sympto](http://www.eurotransplant.org/cms/index.php?page=efretos_report_sympto)

<sup>(165)</sup> [http://www.eurotransplant.org/cms/mediaobject.php?file=brochure\\_efretos\\_def.pdf](http://www.eurotransplant.org/cms/mediaobject.php?file=brochure_efretos_def.pdf)

4. Although the format of the required data set will be tightly specified, flexibility will be needed in the early phase in accepting and converting submitted data to the required formats. It is recommended that any such conversion is performed by the European Registry itself.
5. After data have been submitted to the European Registry, quality assurance procedures should be performed before data are uploaded to the Registry itself.
6. The quality of the Registry data will need to be maintained by updating existing records on a regular basis and making any necessary corrections to the data.
7. A relational database will be required to accommodate the data and website produced that will allow data submission through the Internet.
8. Regular reports that summarise the data held in the European Registry will need to be produced and disseminated.
9. All proposals for audit and research projects based on data held in the European Registry should be scrutinised by a Review Committee set up for this purpose.
10. In the early stages of the formation of the European Registry, a greater number of staff will be needed for setting up the Registry and accepting the first submissions of data from participating countries, but there will be a continuing need for staff to facilitate the uploading of data from countries that join the Registry at a later stage.

Report on the final symposium in Brussel 2011 for presenting the results and conclusions  
<http://www.eurotransplant.org/cms/index.php?page=efretos>

The screenshot shows the Eurotransplant website's page for the EFRETOS project. The header includes the Eurotransplant logo and navigation links like 'Home', 'About Eurotransplant', 'Cooperation', 'What we do', 'Statistics', 'Projects & Themes', 'News', and 'Patients'. The main content area is titled 'EFRETOS' and describes the project's objective: 'The general objective of EFRETOS (European Framework for evaluation of Organ Transplantation) was to evaluate the results of organ transplantation.' It further details the project's scope, funding, and the results presented at a symposium in May 2011. A sidebar on the left provides a quick navigation menu, and a sidebar on the right highlights the project's results, including a report on the symposium, a brochure, and a white paper.

Final Results are available at  
[http://www.efretos.org/images/EFRETOS\\_Deliverable%2011\\_FINAL.pdf](http://www.efretos.org/images/EFRETOS_Deliverable%2011_FINAL.pdf)



### Further information:

EAHC Project Database:

<http://ec.europa.eu/eahc/projects/database.html?prjno=20081101>

Project website

<http://www.efretos.org>

Final Report and Results:

[http://www.efretos.org/images/EFRETOS\\_Deliverable%2011\\_FINAL.pdf](http://www.efretos.org/images/EFRETOS_Deliverable%2011_FINAL.pdf)

### Project team:

Stichting Eurotransplant International Foundation

Plesmanlaan 100

PO-BOX

2332 CB Leiden

NETHERLANDS

Tel. +31 715795704

Fax +31 715790057

### Associated partners:

- Agence de la Biomédecine — ABM, France
- European Society for Organ Transplantation — ESOT, Netherlands
- NHS Blood and Transplant — NHSBT, United Kingdom
- Organización Nacional de Trasplantes — ONT, Spain
- Istituto Superiore di Sanità — ISS/Centro Nazionale Trapianti — CNT, Italy
- ScandiTransplant — SKT, Denmark

Other partners from the Czech Republic, Germany, Greece, Italy, the Netherlands, Poland, Portugal, Slovakia and Slovenia also collaborated in EFRETOS.

### EU contribution

This project has received co-funding from the European Union in the framework of the **Health Programme 2008–2013** (Grant: 20081101).

## European Living Donor Psychological Follow-up (ELIPSY)

*This project has received co-funding from the European Union in the framework of the Health Programme 2008–2013 (Grant: 20081104).*

Information on living donor follow-up is scarce as only a few studies in Europe have been carried out. Furthermore, the interpretation of results is limited due to different methodologies, tools and focuses. The recipient's outcome is an important factor to be analysed, because the psychosocial evolution of living donors could be related to the recipient's outcome. If so, attention should focus on giving the best information to potential donors in the future to prevent that their decision to become a donor may affect in a negative way their quality of life and psychosocial well-being. It is therefore important to study the long-term (1, 3 and 5 years) outcomes of donors and recipient outcomes because most donors make the act of donation for a genetically or non-genetically

related recipient for emotional reasons. The knowledge of negative psychosocial impact in living donors could contribute to better donor selection.

Having a good knowledge and understanding about the living donors' psy-

chosocial outcomes in the long term in the European area that is based on a sound and validated methodology could have an improvement in living donation.

The **main objective of the ELIPSY** project is to contribute to a high quality of living organ donation programmes by creating a follow-up model for the living donors' psychosocial well-being and quality of life. The impact of the recipient's outcome on the donor and the donor's perception of the process will also be evaluated in the follow-up model.

The project has organised its activities in different working groups: WP 4 — Donor Follow-up, WP 5 — Recipient Follow-up, WP 6 — Implementation of the follow-up strategy, and WP 7 — Data analysis and results.

In order to achieve its main objectives, the project carried out the following tasks.

- It designed living donor follow-up tools and methodologies, based on a survey

of current practices, considered the psychosocial well-being, quality of life and perception of the process to evaluate the impact of the donation process on the donor.

- It designed a recipient follow-up methodology, based on a survey of current practices, using the best indicators with the purpose to link the recipient's outcome to the living donor's follow-up.
- It tested the methodology and tools developed in the partners' countries in a prospective study during a period of 15 months. The study was designed to compare the psychosocial well-being and quality of life of the donors before and after donation, and in this way study the impact of the donation process. The impact of the recipient's outcome on the well-being of the donor was also addressed.
- It tested the methodology and tools developed in a retrospective study, assessed the long-term impact of donation and the impact of the recipient's outcome on the donor. Psychosocial well-being, quality of life and the impact of the recipient's outcome data were collected for a period of 15 months from donors who donated 1, 3 and 5 years ago.

### Main outcomes of the project

The main outcomes of the project will include:

- knowledge of current living donor (LD) follow-up practices;
- a standardised LD assessment and follow-up methodology, analysing the donors' perception of the donation process as well as their psychosocial well-being and quality of life;
- a standardised recipient's follow-up methodology, to relate the recipient's outcome in donor's psychosocial well-being and quality of life;
- a strategy for living donor evaluation;

“From December 2009 to October 2012, a consortium of seven partner organisations from six different countries joined their efforts to fulfil the objectives and tasks of the project.”

The screenshot shows the ELIPSY website in a Windows Internet Explorer browser. The address bar displays <http://www.eulivingdonor.eu/elipsy/what-is-elipsy.html>. The website header includes the ELIPSY logo and the tagline: "Living donor psychosocial follow-up strategy and tools for long-term quality and safety in living donor transplantation programs in European Countries." Below the header is a navigation menu with buttons for "What is ELIPSY", "Expected Results", "Working Groups", "The Consortium", "Links", and "News & Events". The main content area is titled "What is ELIPSY?" and contains two columns of text. The left column features a magnifying glass over a globe icon. The right column lists the project's objectives and methodology, including a bulleted list of key activities.

ELIPSY website at <http://www.eulivingdonor.eu/elipsy/>

- contribution to the harmonisation in the European area of Living Donation assessment/follow-up studies that contribute to a high quality of living donation programmes.

Expected project impact, as seen by the project partners, emphasises that developing standard tools and methods will harmonise in the European area the living donor follow-up studies. The tools and methodology will allow the detection of possible negative psychosocial consequences of the living donor related to the recipient's outcome. Knowing the risks, in return, will make it possible to act and take measures to prevent them. This will contribute to guarantee health and safety in psychosocial terms

of living donors through the contribution to the harmonisation of such activities in Europe.

The final meeting of the ELIPSY project was held in Barcelona on 17–19 October 2012. The ELIPSY project website has been set up and included in the platform, which was created for the EULID project. The project results have been disseminated in international conferences inside and outside of Europe such as:

- 2<sup>nd</sup> ELPAT Congress, April 2010, Rotterdam, the Netherlands;
- Living kidney donor follow-up: State of the art and future directions, September 2010, Washington, United States;

- EEUU, European Organ Donation Congress, 22nd ETCO, September 2010;
- ELPAT Meeting, October 2010, Sofia, Bulgaria.

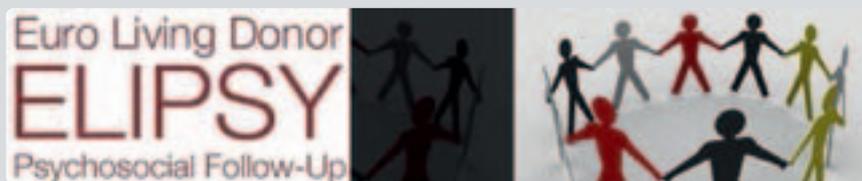
The project was also been invited to present its interim results during the Competent Authorities meeting in Brussels that was held from 28 February–1 March 2011. Please visit the ELIPSY project website for further information at [www.eulivingdonor.eu](http://www.eulivingdonor.eu) where reports will be made available after finalisation.

### Results and Conclusions

- The study used the EULID registry, an on-line database developed within a project during 2007-2009 with more than 1400 living donors registered.
- The first survey showed no previous consensus in the Living donors psychosocial assessment and follow-up practices among the studied transplant centres.
- There was an unification of the most relevant psychosocial variables to be assessed and follow-up.
- The same tools will be used to evaluate the Living donors aspects Quality of life, Psychosocial wellbeing and Satisfaction with the donation process.
- Each of the centres translated the tools in their own language and adapted the methodology to their characteristics and resources.
- The prospective study linked post donation mental health and psychosocial wellbeing of living donors and their satisfaction one year after donation to their psychosocial profile before donation.
- The retrospective study identified the long term impact of living donation in terms of mental health, psychosocial wellbeing and satisfaction after donation process.
- The impact of recipient outcome in the living donor is evaluated in both studies.
- The donors assessed demonstrate to have absolute Psychosocial well-being and Quality of Life.
- All the centres who follow similar methodology are considered as excellence level centres.

### Acknowledgments

**The first gratitude goes to all the Living donors who participate in this study. Their participation allowed the realization of the project. A very special thanks goes out to all participants in all the stages of the project. We hope to have contributed with this project to a better care of Living donors.**



### Further information:

EAHC Project Database:

<http://ec.europa.eu/eahc/projects/database.html?prjno=20081104>

Project website

<http://www.eulivingdonor.eu/elipsy/>

### Project team:

Hospital Clinic i Provincial Barcelona  
C/ Villaroel, 170  
PO-BOX  
08036 Barcelona  
SPAIN  
Tel. +34 932275713

### Associated partners:

- Hospital Geral de Santo Antonio, Portugal
- Hospital Necker, France
- Paraskevaïdion Surgical and Transplant Service (until 31 December 2010), Cyprus
- Rikshospitalet-Radiumhospitalet Medical Center (until 1 January 2010), Norway
- Sahlgrenska Universitetssjukhuset Hospital, Sweden
- Charity Universtätsmedizin Berlin (from 1 January 2010), Germany

### EU contribution

This project has received co-funding from the European Union in the framework of the **Health Programme 2008–2013** (Grant: 20081104).

## Developing Guidelines for the Organisation of a Public Organ Donation Day (EDD)

*This project has received co-funding from the European Union in the framework of the Health Programme 2008–2013 (Grant: 20081109).*

Transplantation medicine is dynamically developing with enormous progress and great successes in recent decades. The major challenge however in this field is the shortage of available organs. According to the estimates of the Council of Europe, more than 56 000 people are on different transplantation waiting lists. The donation rate greatly varies among EU Member States.

**The Council of Europe organises the European Day of Organ Donation and Transplantation each year in different host countries amongst its member states**

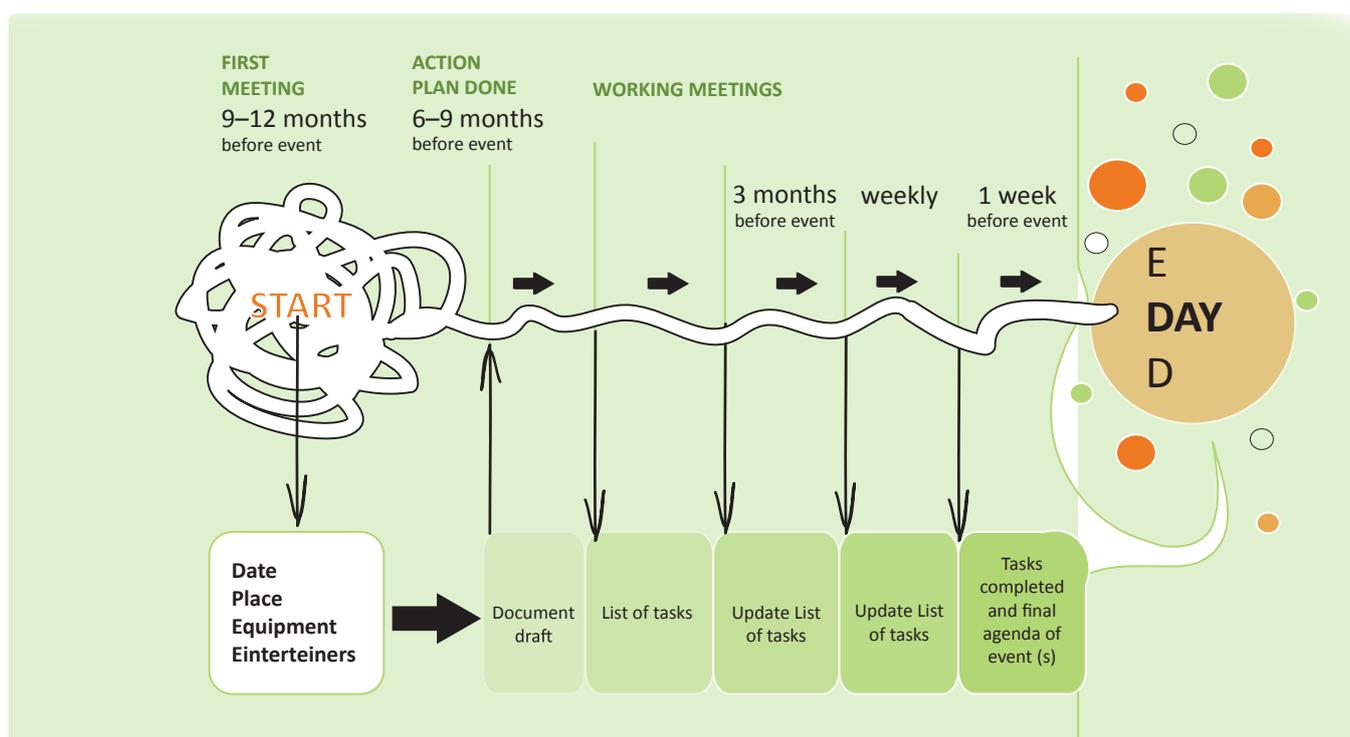
The Council of Europe organises the European Day of Organ Donation and Transplantation each year in different host countries amongst its member states. The concept of accompanying so-called satellite celebrations grew into equally important simultaneous events. Traditionally, the European Donation Day has been held in October.

*“Transplantation is a unique moment in the medicine, where life of the patient depends on a wish or will of another person.”*

*Prof. Philippe Morel, founder of European Donation Day*

The Action Plan on Organ Donation and Transplantation by the European Commission states a number of priorities to improve donation rates, among others public awareness. The European Donation Day is increasingly seen as one primary European awareness-raising event about organ and tissue donation and transplantation.

The project EDD was coordinated by Slovenia-Transplant, the associated and collaborated partner organisations were from Austria, Croatia, Slovakia, the Czech Republic, Montenegro, Republic of Serbia, the Federation of Bosnia and Herzegovina and Georgia, and two supranational organisations, the European Directorate for the Quality of the Medicines — Council of Europe — and Eurotransplant International



*Timeplanning for the organisers of an awareness-raising day, such as the EDD*

Foundation. The EDD project started in September 2009 and lasted for 20 months.

The main partner of the EDD project in 2008 organised an event on behalf of the Council of Europe in Ljubljana. Slovenia-Transplant developed a model on how to organise such a European Donation Day and which components to organise based on its own experiences in organising this event in 2008. This model is proposed to be modified according to different cultural circumstances and formulated into general guidelines that can help organise future European Donation Days in European Member States with less developed organ donation awareness.

### The main objective of the EDD project was to develop and disseminate guidelines for the organisation of future European Donation Days

The **main objective** of the EDD project was to develop and disseminate guidelines for the organisation of future European Donation Days, elaborated by consultation of experts and considering the guidance of the Council of Europe, the initiator of the main event. Furthermore, the idea was to test, whether satellite European Donation Days in parallel to the main event are beneficial for raising awareness on organ donation in the specific circumstances of small countries.

### The project activities were organised in three major work packages

The first aimed to **outline the guidelines for organising** European Donation Days in a way to include practical recommendations and tips on the organisation and on a methodology for measuring the awareness-raising potential of such events. In order to fulfil these tasks, expert meetings together with a final consensus conference were held to finalise the guidelines and the methodology.

The second was to **test the feasibility of the guidelines** by organising satellite European Donation Days in different locations. These satellite events were organised during the project in Slovenia, Austria, Croatia, the Czech Republic and Slovakia in parallel with the main event.

“ *A unified European Donation Day on organ and tissue transplantation could help raise public awareness, enhance a positive attitude towards organ donation and potentially augment the number of organ donors.* ”

EDD toolkit

SATELITSKO  
PRAZNOVANJE  
EVROPSKEGA DNEVA  
DAROVANJA V SLOVENIJI

Vabljeni v Tivoli  
Dobrodelni tek, hoja in ustvarjalne delavnice  
za življenje in radost

Sobota, 16. oktober 2010  
Jakopičev drevored v Tivoliju  
Ljubljana

Tecimo in hodimo!  
10.30 Zadnje prijave za tek  
11.30 Start teka na 8 km  
11.30 Start hoje na 2 km

Ustvarjajmo!  
10:30 - 14:00 otroci ustvarjajo...

SLOVENIJA  
TRANSPLANT

Podrobnejše informacije na  
[www.Slovenija-transplant.si](http://www.Slovenija-transplant.si)

© EDDM, Council of Europe. Vse pravice pridržane.

Ta dokument/dogodek je del projekta «Razvijanje smernic za organizacijo Evropskega dneva darovanja», ki ga financira Evropska Unija v okviru Zdravstvenega programa (<http://ec.europa.eu/eahc/>). Svet Evrope je pobudnik ideje praznovanja Evropskega dneva darovanja organov in transplantacij. Ni je namenjen spoštovanju razprav na tem področju in ozaveščanju ter napredku na področju darovanja in presajanja organov. ([www.edqm.eu](http://www.edqm.eu) in [www.coe.int](http://www.coe.int))

Poster for the EDD Satellite day in Slovenia, 2010



Selected works of the high-school children produced during the art competition (EDD toolkit) 'Monolith' by Cornelia Brandstetter. Without title. Daniela Wöckinger. Man, enveloped by darkness, crouching, threatened, in need of help. The artist depicts man, ornamentally disintegrated as a symbol of dejection and despair. The heart as a symbol of love gives trust. Living love by donating a heart. Life conquers death.

The experiences of organising these events were drawn up in a report and provided further information to the finalisation process of the guidelines.

“One of the most important factors that influences the organ donation rate is social awareness.”

EDD toolkit

The third was to **measure the awareness-raising potential** of the applied guidelines. The project partners designed a survey which was administered by a professional opinion research organisation IPSOS Marketing in the above five countries before and after the satellite European Donation Days. Questions about the public information, knowledge and opinions on organ donation and awareness of the European Donation Day celebration were asked. In each country a sample of 700 respondents, representative of gender, age and region, was used.

**In each participating country a sample of 700 respondents, representative of gender, age and region, was interviewed twice**

The EDD project has managed to further develop and validate the protocol that Slovenia Transplant successfully implemented during the European Donation Day organised in Ljubljana in 2008. During the EDD project the effects on populations of various states inside and outside of the EU were measured and compared, leading to useful conclusions and recommendations.

The results of the European Donation Day surveys conducted in 2010 by the project showed that the celebration not only sensitised the public, but also informed them in significant ways about organ donation.

The major findings of the survey showed that after the European Donation Day in 2010:

- the public received more information on organ donation;
- information on some particular subjects regarding organ donation was better disseminated;
- awareness of the European Donation Day celebration among the general public was higher;
- a part of the general public obtained new and interesting information about organ donation; new information influenced their opinions, feelings and decision-making in a positive way.

### The main output of the project is the EDD Guideline — European Donation Day Toolkit for Event Organisers

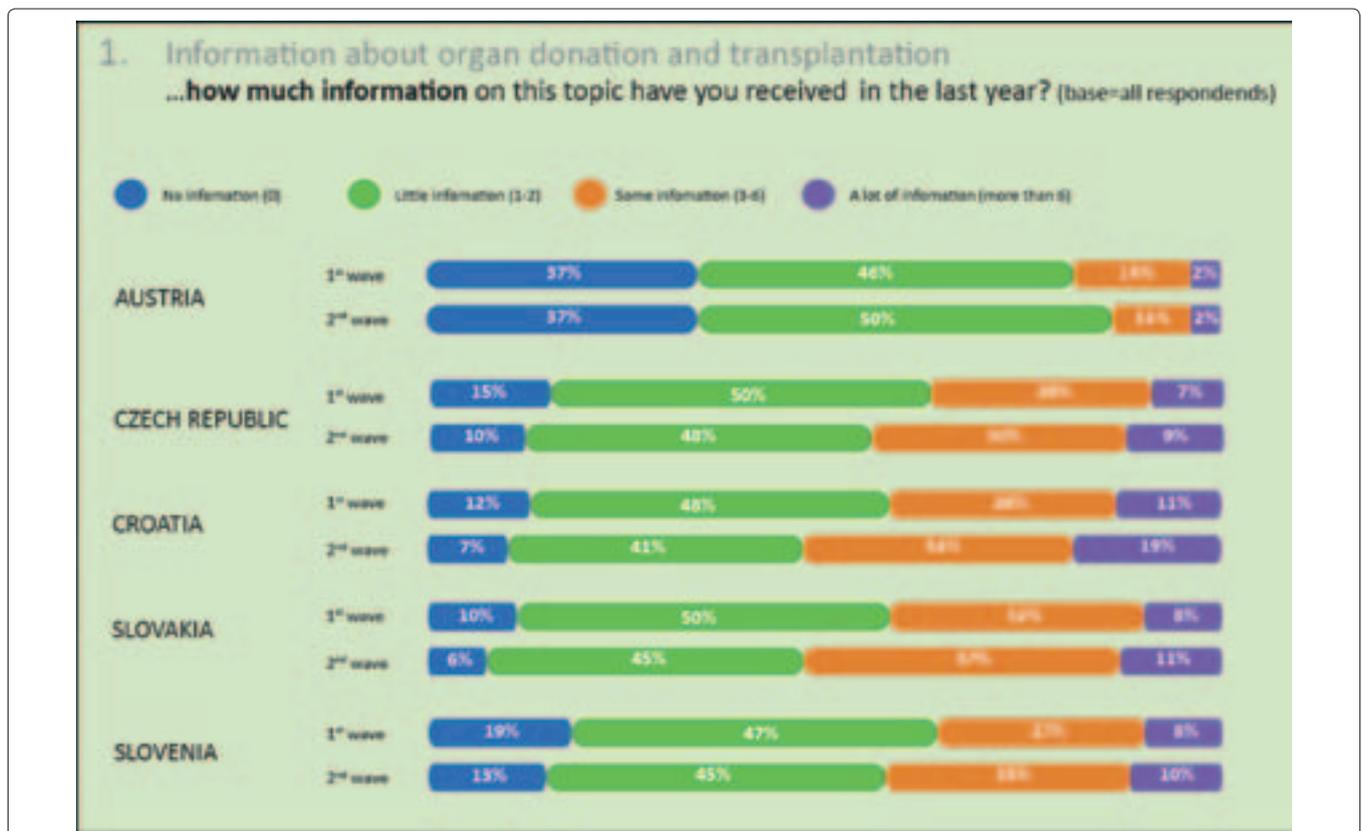
As no extensive guidelines for the organisation of the European Donation Day existed before, the toolkit developed by the project fills this gap and shares important lessons learned.

The guidelines and toolkit are intended to help and support future organisers of the European Donation Day events. The toolkit has been developed for healthcare professionals, educational organisations, institutions and governmental agencies interested in organising European Donation Day. Policymakers at all levels will also find the guide useful when spreading the message regarding organ and tissue transplantation and donation.

The toolkit gives plenty of practical suggestions, ideas and possible strategies to adapt a European Donation Day to the organisational needs and financial possibilities of the event future organisers. During the development of the guidelines, the political, economical and cultural specifics of different countries have been taken into consideration as well.

According to the toolkit, the main objectives of a unified European Donation Day are:

- to raise public awareness in the field of organ and tissue donation and transplantation;
- to acknowledge all the people involved in the transplant process (transplant patients



The amount of information received on organ donation and transplantation in the last year: comparison of the results (before first wave/after second wave) in all participating countries (EDD Toolkit)



*The Toolkit for Event Organisers — European Organ and Tissues Donation Day.  
The brochure is available in print and electronic format.*

- and their families, organ donor families, healthcare professionals);
- to establish trust among the general public towards responsible, ethical, non-commercial and professional organ and tissue donation and transplantation;
- to share and discuss challenges and innovations in transplant medicine among healthcare professionals;
- over the long term to increase the number of organ and tissue donors.

*“Promotion of the European Donation Day event should stress the fundamental principles of organ donation and transplantation: solidarity, non-profit orientation, social awareness, gratitude and compassion.”*

EDD toolkit

*‘This publication presents guidelines, instructions and recommendations for organising an EDD. It fills an important gap in this field at the European level. The publication addresses, in an appropriate and up-to-date way, social actors who ought to be acquainted with the*

*importance of celebrating European Donation Day as well as of donor activities themselves. Through this publication on EDD and the organisation of events, the trust, importance, and humanity of organ donation is additionally emphasised. The toolkit is a professionally prepared and well-designed booklet which will also be of interest to other organisers of similar events,' explains Prof. Dr Eldar M. Gadžijev as an introduction at the webpage, where the toolkit can be downloaded for free (see infobox below).*

### Dissemination of project results to stakeholders

The toolkit was printed and distributed in 750 copies, while electronic copies were distributed to an international group of approximately 1 400 stakeholders. The project has set up and maintains a website where all project related documents and resources are available ([www.europeandonationday.org](http://www.europeandonationday.org)) for those who are planning to organise a Public Awareness-Raising Day in Organ Donation, such as the European Donation Day.



*Slovenian Prime Minister Borut Pahor (centre) expressed his commitment and support to organ donation by participating in the event 'Run for life and joy' (EDD Toolkit)*

## EUROPEAN DONATION DAY Toolkit for Event Organizers

### Further information:

EAHC Project Database:

<http://ec.europa.eu/eahc/projects/database.html?prjno=20081109>

Project website

<http://www.europeandonationday.org/>

The toolkit:

[http://www.europeandonationday.org/index.php?option=com\\_content&view=article&id=5&Itemid=7](http://www.europeandonationday.org/index.php?option=com_content&view=article&id=5&Itemid=7)

### Project team:

Zavod R Slovenije za presaditve organov in tkiv Slovenija-transplant

Zaloška Cesta 7

PO-BOX

1000 Ljubljana

SLOVENIA

Tel. +386 13006862

Fax +386 13006866

E-mail: [danica.avsec@slovenija-transplant.si](mailto:danica.avsec@slovenija-transplant.si)

### Associated partners:

- Austria Transplant, Austria
- Czech National Coordinating Centre, Institut Klinicke a Experimentalni Mediciny, Czech Republic
- Ministry of health and social welfare Republic of Croatia, Croatia
- Martin Faculty Hospital Dept of Transplant and Vascular Surgery, Slovakia

### EU contribution

This project has received co-funding from the European Union in the framework of the **Health Programme 2008–2013** (Grant: 20081109).

# European Quality System Indicators and methodology on Organ Donation (ODEQUS)

*This project has received co-funding from the European Union in the framework of the Health Programme 2008–2013 (Grant: 20091103).*

Important differences exist in the national donation deceased and live donation rates and in the effectiveness of donation programmes among the European countries.

This implies that European citizens have different chances to undergo organ transplantation depending on where they live. These differences can be partly explained by the type of donation programmes implemented but other issues such as the organisational structure of their donation services, their efficiency and social factors have also been seen to have considerable impact.

Previous best practices analysis in organ donation show that evaluation tools are an important part of quality systems. Their utilisation should ultimately increase the number of citizens attending the European donation programmes, regardless of economic, legal or cultural differences.

## ODEQUS intends to increase the efficiency of organ donation in European hospitals by creating useful evaluation tools

The ODEQUS — Organ Donation European Quality System — project intends to increase the efficiency of organ donation in all European countries by creating useful evaluation tools. The project is the joint effort of 14 associated partners and five collaborating partners, including altogether 16 countries from Europe. It is coordinated by the University of Barcelona. The project spans from October 2010 until September 2013.

Therefore the general objective of ODEQUS is to determine the standards of best practices and to develop quality indicators for donation after brain death (DBD), donation after cardiac death (DCD) and living donation (LD) in order to create tools to evaluate the overall quality in organ donation.

The project is working in the following areas to set up the quality indicator system:

- to identify and develop quality criteria in the three different types of organ donation

(DBD, DCD and LD) focused mainly at hospital level;

- to create quality indicators in order to assess organisational structures, clinical procedures and outcomes on the three types of organ donation;
- to develop auditing tools in order to evaluate the implementation of best practices described in the quality criteria and used by the quality indicators;
- to train healthcare professionals on how to use the quality indicators and the auditing tools.



## Quality Criteria

Version May 2013

A draft of the quality criteria developed by ODEQUS is already available on the project website ([http://www.odequs.eu/pdf/odequs\\_quality\\_criteria.pdf](http://www.odequs.eu/pdf/odequs_quality_criteria.pdf))

The ODEQUS tools created are designed to be wide enough to be implemented in different target hospitals and may be later exported to other European countries.

### The ODEQUS tools created are designed to be wide enough to be implemented in different target hospitals

The ODEQUS activities so far have identified and systematised the standards on best practices in the three types of organ donation, through literature review, research for evidence based on best practices and the performance of a comparative/benchmarking study. Results have been compiled in the comparative study report and on a quality criteria document. A draft of the quality criteria developed by ODEQUS is already available on the project website ([http://www.odequs.eu/pdf/odequs\\_quality\\_criteria.pdf](http://www.odequs.eu/pdf/odequs_quality_criteria.pdf)).

### ODEQUS has developed and created the quality indicators on organ donation services organisational structures and clinical procedures

ODEQUS has developed and created the quality indicators (QIs) on organ donation services

organisational structures and clinical procedures, based on the comparative study and quality criteria (QCs). The fields taken into account for measuring the organisational structures have been: legal framework, accreditation and certification, organisation, human resources (job description — core competences), material resources (office, equipment, etc.), finances (sources/payment), services offered, marketing for improving outcomes, media/dissemination (information systems), education and research.

Clinical process related to the three types of organ donation have been considered as following: donor identification; clinical evaluation; death diagnosis; family/personal consent; donor maintenance; organ viability evaluation and placement, surgical organ recovery; organ preservation; number of donors, organs and number of transplants.

### A 2-day training course on quality indicators has been developed

A 2-day training course on quality indicators was developed and implemented for 11 people in Lisbon (Portugal) on April 2011. The trainings are to enable them to document the QS, to create the QI, and use the evaluation tools. After the implementation of QS and QI in the respective



ODEQUS website at <http://www.odequs.eu/>

hospitals, an external evaluation will be done in at least one participating donation service.

A further step in the ODEQUS project is to organise the next training course in October in Lisbon, Portugal. The audits are planned to be implemented from October to December in 2012.

### The ODEQUS project targets a wide range of stakeholders and target groups with its results

The ODEQUS project targets a wide range of stakeholders and target groups with its results: national health authorities, NGOs, donor hospitals, transplant centres and coordinators, tissue banks, critical care members, ethicists, physicians, patient associations, pharmaceuticals, insurance companies, specialised and general media, donors, donor's families, waiting candidates, recipients and citizenship.

The project website is available at [www.odequs.eu](http://www.odequs.eu) where main outputs will be available. A layman brochure has been developed and distributed. The ODEQUS project has been introduced and its results disseminated in different congresses and international meetings, as well as in competent authority meetings. The final meeting of ODEQUS was held at the end of May 2013 in Barcelona.



- Associated partners
- Collaborating partners

*Partners in the ODEQUS project*

## Objectives

The main objective of the ODEQUS Project is to define a methodology to assess the performance of organ procurement at hospital level.

More specifically, other objectives of the project are:

- ✓ to identify and develop Quality Criteria (QC) in the 3 different types of organ donation (DBD, DCD and LD) focused mainly at hospital level;
- ✓ to create Quality Indicators (QI) in order to assess the organizational structures, clinical procedures and outcomes on the 3 types of organ donation;
- ✓ to develop auditing tools in order to evaluate the implementation of best practices described in the QC and used by the QI;
- ✓ to train healthcare professionals on how to use the QI, checklists and auditing procedures.

*Objectives of the project*



### Further information:

EABC Project Database:

<http://ec.europa.eu/eabc/projects/database.html?prjno=20091108>

Project website

<http://www.odequs.eu/>

### Project team:

Universitat de Barcelona — UB  
 Gran Via de les Corts Catalanes 585  
 PO-BOX  
 08007 Barcelona  
 SPAIN  
 Tel. +34 934037687  
 Fax +34 931986076

### Associated partners:

- Agence de la Biomédecine, France
- Autoridade para os Serviços de Sangue e da transplantação — ASST, Portugal
- Deutsche Stiftung Organtransplantation — DSO, Germany
- Donation Transplant Institute, Spain
- Fondazione per l'incremento dei Trapianti d'Organo e Tessuti Onlus, Italy
- Fundatia Pentru Transplant Romania, Romania
- Karolinska Institute, Sweden
- Medizinische Stiftung Universität Wien — MUW, Austria
- Ministry of Health and Social Welfare Republic of Croatia, Croatia
- NHS Blood and Transplant, United Kingdom
- Polish Transplant Coordinating Centre, Poland
- Fundacion Investigacion Biomedica Hospital Gregorio Maranon, Spain
- Fundació Bosch I Gimpera — FBG (from 16 December 2010), Spain
- Servicio Madrileño de Salud — SERMAS (from 16 August 2010), Spain

### EU contribution

This project has received co-funding from the European Union in the framework of the **Health Programme 2008–2013** (Grant: 20091108).

# Coordinating a European Initiative among National Organisations for Organ Transplantation (COORENOR)

*This project has received co-funding from the European Union in the framework of the Health Programme 2008–2013 (Grant: 20091103).*

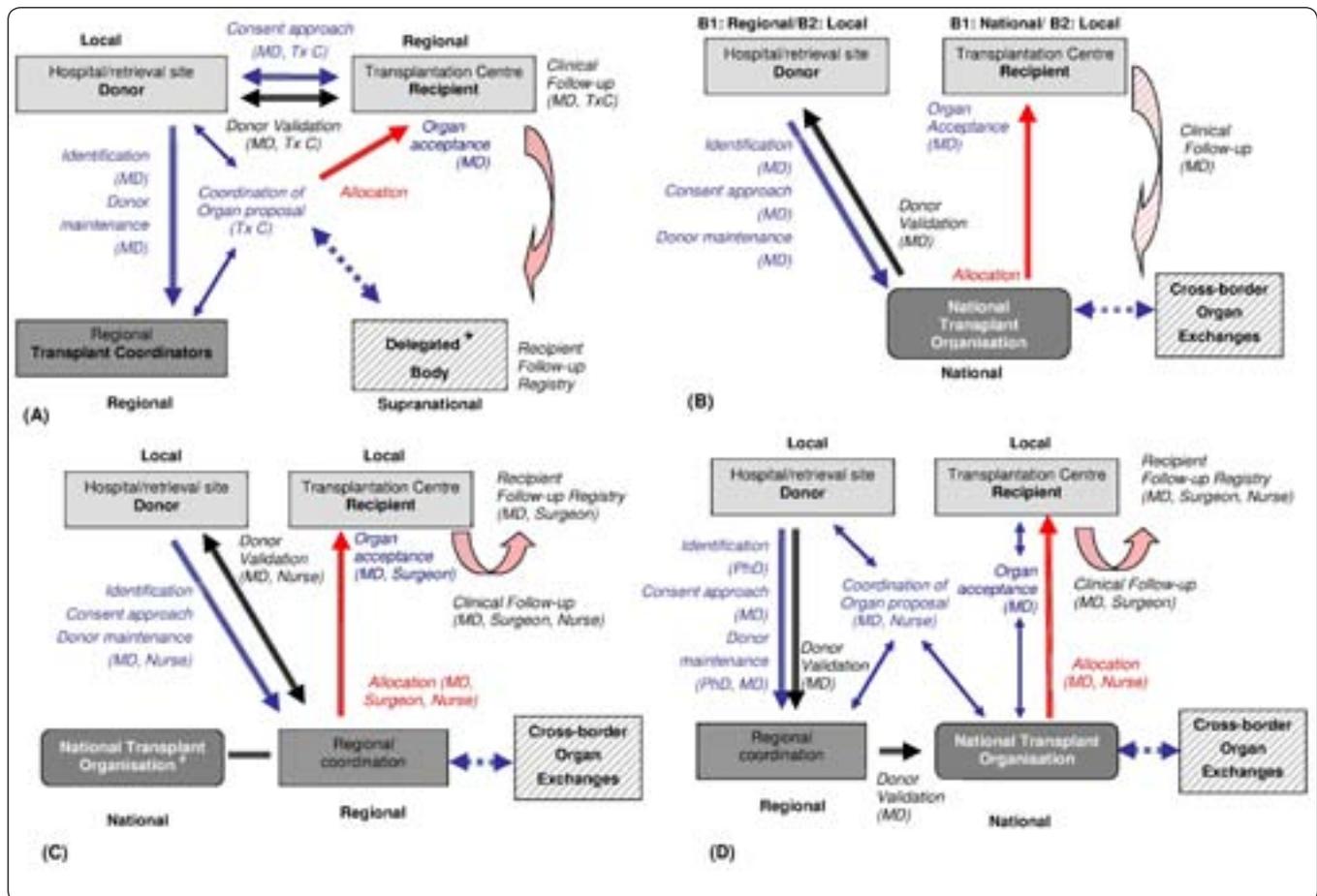
Donation and transplant programmes and rates greatly differ in the Member States of the European Union. Some countries have established systems, other have less experience in this field. Furthermore, not all programmes are available in all countries. This creates inequality in access to transplantation for patients in the various countries. The differences in the way the countries organise their donation and transplantation processes could be a reason for such a varying picture in accessibility and outcomes.

To face such challenges, the COORENOR project's general aim was to establish a coordinated network between national programmes

in organ transplantation in the participating EU countries, focusing on specific activities in major issues such as deceased donation, living donation and cross-border organ exchange.

Altogether 13 organisations from 10 different countries, the majority of which are from the new EU Member States, have joined their efforts to implement the COORENOR project from June 2010 until December 2012. The project was coordinated by the Italian National Transplant Centre.

In order to reach the project objectives, partners have organised project activities in four core work packages.



**Figure 1: Representative transplant systems: main organisational and responsibility levels (systems A, B: B1/B2, C and D).** \*: Delegated body is also in charge of cross-border exchanges out of members, when required. #: National transplant organisation being more or less involved, depending on the Member State concerned. Tx C: Transplant coordinator. MD: Medical doctor. PhD: Doctor in science. The coordination of organ proposal stands for a common action of actors involved. Cross-border organ exchanges being dealt either with national or supranational transplant organisations (Agence de la biomédecine, COORENOR, 2012, ESRI).

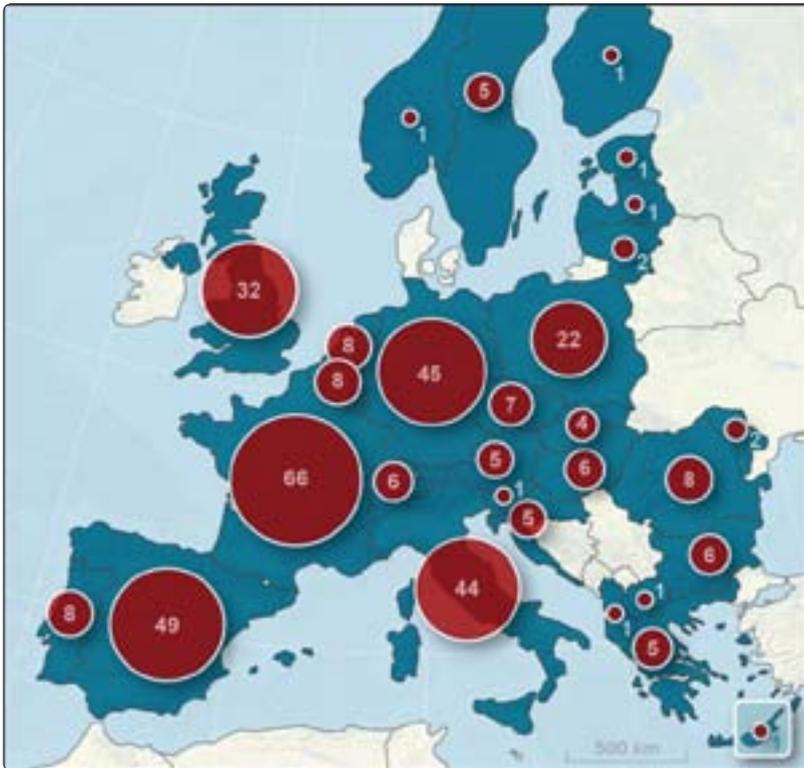


Figure 2: Number of hospitals performing transplantation in 2010 (including those authorised for such activities but that were non-active that year; Agence de la biomédecine, COORENOR, 2012, ESRI).

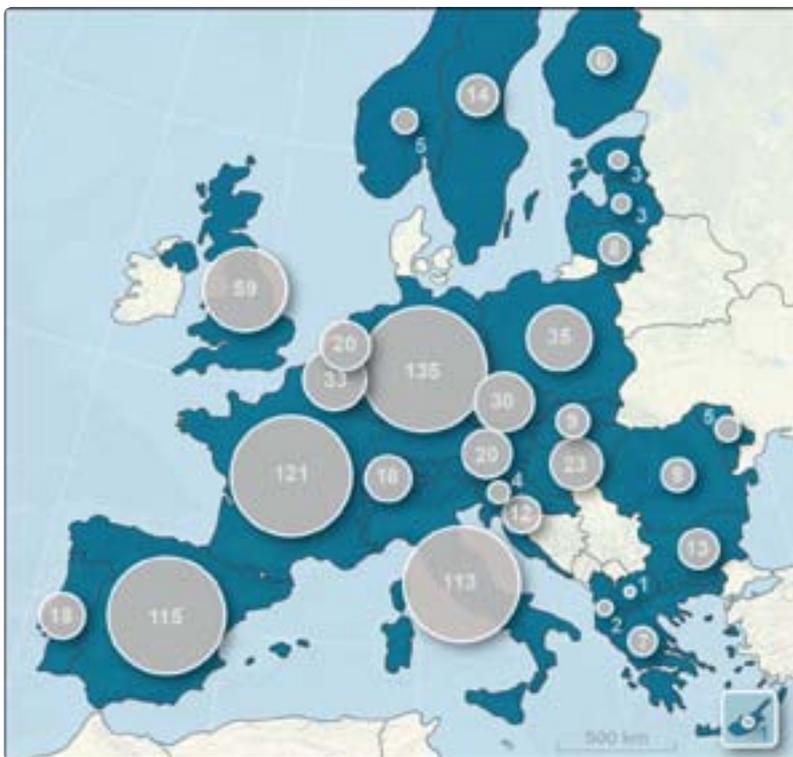


Figure 3: Number of transplant teams/programmes in 2010 (including those authorised for such activities but that were non-active that year; Agence de la biomédecine, COORENOR, 2012, ESRI).

### Investigating, comparing and benchmarking national/regional transplantation programmes

Building on the main outcomes of earlier projects such as the ALLIANCE-O project (see pages 141–145), partners surveyed the Member States, acceding states and other selected countries, altogether 35, on their existing transplant programmes. A comprehensive overview is on the way to help create a complete picture of some fundamental mechanisms in the organisation of transplantation systems in these countries with a special focus on the new EU Member States.

A profile for each country is under preparation where, in addition to general country information, all the pivotal details on transplant programmes such as how countries organise, regulate and fund their transplant system will be included. *'The overview also gives useful information on the implementation and the transposition of the Directive 2010/53/EU and the Action Plan,'* says Paola Di Ciaccio, project coordinator, Head of Foreign Affairs Division at the Italian National Transplant Centre (Fig. 1).

Additionally, a European benchmarking programme is being developed by the project. This process started with identifying a set of indicators, along which the programmes can be compared and achievable benchmark models can be identified (Fig. 2, 3).

Finally, recommendations on further initiatives and future work are being prepared on the challenges of issuing common European Guidelines on different aspects of organ donation and transplantation (i.e. organisational strategies and educational methodologies).

### Deceased donation: cerebral death assessment, procurement, safety and quality, allocation and outcomes

This work has focused on the analysis of existing systems regarding scientific aspects of deceased donation. The starting points of this work were the results of earlier projects such as the ALLIANCE-O and DOPKI. Information was collected via three questionnaires from the then 27 European Union Member States and two international organisations (Eurotransplant and Scandiatransplant).

The first survey and analysis focused on laws and/or protocols concerning the diagnosis of brain and cardiac death and critical steps related to deceased donation in all EU countries. Special effort was made to highlight possible differences in daily practice of the identification of potential donors and the diagnosis of death. 'This work will give useful information to a new joint action named ACCORD, which has a work package devoted to the end of life care pathways that can lead to organ donation,' explains Paola Di Ciaccio.

The second survey and analysis have focused on public awareness campaigns regarding deceased organ donation and their impact on organ donation.

The third survey and analysis assessed the organisational aspects of existing programmes. The output here was an overview of medical centres accredited to organ transplantation, the training of healthcare professionals and existing quality assurance programmes.

“The project could successfully reach competent authorities, who are managing the Action Plan, on different subjects to work together and build a network among them. We expect that sharing possible solutions for common problems and good practices can bring the desired improvements.”

Alessandro Nanni Costa, scientific project leader, general director at the Italian National Transplant Centre

The screenshot shows the COORENOR website interface. At the top, there is a navigation bar with 'Dashboard', 'COORENOR', and 'Home' links, along with a search bar and a 'Browse' dropdown menu. Below the navigation bar, the COORENOR logo is displayed, followed by a 'Home' heading and a 'Share' button. A sidebar on the left contains a menu with items: Home, Organ Exchange Application, International, National, Links, Discussion forum, Education, Events, and Help & FAQ. The main content area features a large heading: 'Welcome in COORENOR - WP7 Crossborder organ exchange!'. Below this heading, there is a section titled 'COORENOR - WP7 Crossborder organ exchange' with a detailed paragraph describing the project's purpose and structure. To the right of this section is a 'Recent news' box containing a news item titled 'Prague baby's heart saves life of little girl from Rome - press by Miral'. At the bottom of the page, there is a row of circular icons representing various European countries, and a 'Public Health' logo is visible in the bottom left corner.

Figure 4: IT portal for cross-border organ exchange



Figure 5: COORENOR main deliverables

### Living donation: maximising the safety of living donors

The main goal of this work is to develop a common European strategy aiming to increase living kidney donor transplantation. The then 27 EU Member States were surveyed about many different aspects of living donation to be able to give a comprehensive overview of living organ donation practices. Issues included legal regulations, organisational structure and medical providers, evaluation of living donor, the use of extended categories of living donors, methods to reduce surgical donor's complications, long-term follow-up of living donor, risk assessment and pre-emptive management to prevent donors complications, ethical and social consideration regarding living organ donation.

The work performed also included the organisation of a scientific expert meeting in June 2011 in Warsaw where the results of the survey was presented and participants discussed the possible recommendations for the strategy.

### Cross-border organ exchanges

In European countries where no supranational organisations are devoted to organ exchange practices, organ exchange takes place on a voluntary basis or through bilateral agreements. Additionally, no information is collected about organ exchange activities, on surplus and demand on international level.

The aim of this COORENOR work package was therefore to provide a comprehensive overview of cross-border organ exchange for transplantation with a special focus on existing legal regulations on organ exchange and the financial, organisational and logistical aspects. This work package also aimed to develop the main outline of an IT registry tool to serve international collaboration in organ exchanges.

The project asked the then 27 EU Member States and international organisations to provide data on a wide range of issues in organ exchange activities such as cross-border and international organ exchange policies; number and type of organs exchanged and features of donors and recipients; existing organ exchange agreements; and presence and role of national/international organisations responsible for cross-border organ exchanges.

In addition to providing the first comprehensive picture of the international organ exchange practices in Europe, the work highlights the various problematic aspects of the present cross-border organ exchange practices.

In order to support international organ exchange, the main features of an IT platform were identified. The IT application is presently running among project partners. The platform was designed to be user-friendly, to be able to connect organ supply with demand in a quick and safe electronic manner, and to be cheap as far as costs for maintenance are concerned.

A basic set of necessary information to be uploaded on organ offers and possible demand was also identified by the project (Fig. 4). The IT platform for cross-border organ exchange will be further developed in the framework of the Joint Action FOEDUS..

### Spreading the results of the COORENOR project to the main stakeholders

Information on the project is available on the project website [www.coorenor.eu](http://www.coorenor.eu). The main COORENOR results and outputs are available here for the public. The COORENOR Laymen Brochure<sup>(166)</sup>, available both electronically and in printed format, has been disseminated among partners for local information provision. Two layman's brochures on deceased organ donation and living kidney donation were prepared and translated to national languages in countries where organ donation is less developed, namely Latvia, Lithuania and Romania.

The general structure of the IT portal for organ exchanges and the preliminary results of the whole project have been widely disseminated during Competent Authority and CD-P-TO meetings. Furthermore, the COORENOR project was presented among the success stories of the Public Health Programme at the High-Level Conference 'EU Health Programmes: results and perspectives, in Brussels, 3 May 2012, organised by the European Commission's DG SANCO and its Executive Agency. *'Several posters have been prepared for the European Health Forum Gastein and for other international meetings, to disseminate COORENOR results to high-level policymakers and to the general public'*, explains Paola Di Ciaccio.

The project ended on 24 December 2012 and all the results were presented during the final meeting which was hosted in Budapest by the leader of the dissemination WP.

### Main results, expected impact and added value for EU citizens

COORENOR has generated comprehensive knowledge on the current situation of organ donation and transplantation in the wider

### Organ exchanged through the web portal, 20 November 2012

The COORENOR portal started running on 1 July 2012 and some partners have successfully started using this tool for offering surplus organs to all involved organ exchange organisations working in Europe, thus increasing the possibility to avoid wasting useful resources and the chances of patients to be transplanted.

The first success of the portal was the exchange of a heart of an infant from Prague that saved the life of a baby girl in Rome in last August, thanks to this European system of quick sharing of information on available human organs.

When a 1-year-old child died in Prague in early August, his parents gave consent to his organs being donated to patients who may need them and since no suitable recipient was present on the national waiting list, the doctors entered the relevant data in the COORENOR Internet-based system presenting offers and demands for human organs from participating countries.

The Italians were the first to react through the Italian Gate to Europe office.

*'We received an answer from Rome in a minute after publishing our offer,'* told Pavel Brezovsky, head of the Czech Transplant Coordinating Centre (KST). On Monday night, a private plane with a surgical team arrived in Prague, and on Tuesday morning the Czech infant's heart was given to an 11-month-old patient in Rome who had waited for a heart since April. A mere 27 hours elapsed between the offer's entry in COORENOR and the surgery in Rome.

A new successful exchange was performed on October 30, 2012. A COORENOR donation alert was launched by Polish transplant organisation, Poltransplant. The donor was a 4-year-old male that had died in Krakow due to a brain hemorrhage. The Italian Gate to Europe coordination staff reacted first to the alert and the liver and two lungs were accepted by some Italian transplant centres. The Bergamo Transplant Centre split the liver to allow two transplants: the left liver part was transplanted in a 1-year-old baby and the right part in a 4-year-old child, both patients on a waiting list at Bergamo Transplant Centre. The lungs were retrieved by the Padua Transplant Centre and the same team transplanted them in a 9-year-old child. All the transplants were successfully performed with the functional recovery of the organs.

*News from the COORENOR website on the successful start of the organ exchange platform (<http://www.coorenor.eu/>)*

Europe and identified possible common European pathways for improvement. Project results are expected to contribute to the improvement of overall quality and safety of transplants in the European Union, to better traceability of international exchanges and visibility of competent authorities in Member States.

*'The project could successfully reach competent authorities, who are managing the Action Plan, on different subjects to work together and build a network among them,'* says Alessandro Nanni Costa, scientific project leader, general director

<sup>(166)</sup> Available on the project website: <http://coorenor.eu/images/stories/download/coorenor.pdf>

at the Italian National Transplant Centre. *'We expect that sharing possible solutions for common problems and good practices can bring the desired improvements'* (Fig. 5).

Furthermore, *'In Europe, organ donation and exchange is part of public life under public rules. The results of COORENOR — respecting the various organisations, agencies and authorities — can contribute to these public rules and help raising better public awareness about national transplantation programmes, the problems and possible solutions,'* shared Mr Nanni Costa on his thoughts on the added value of COORENOR for European citizens.



### Further information:

EAHC Project Database:

<http://ec.europa.eu/eahc/projects/database.html?prjno=20091103>

Project website

<http://www.coorenor.eu/>

### Project team:

Centro Nazionale Trapianti (CNT)  
Istituto Superiore di Sanità — ISS  
Viale Regina Elena 299  
00161 Rome RM  
ITALY  
Tel. +39 0649904040  
Fax +39 0649904101  
E-mail: [centronazionale.trapianti@iss.it](mailto:centronazionale.trapianti@iss.it)

### Associated partners:

- Agence de la biomedecine — ABM, France
- Eurotransplant International Foundation — ETI, Netherlands
- Gesundheit Österreich GmbH — ÖBIG (until 15/11/2010), Austria
- Fundeni Clinical Institute — FCI, Romania
- Koordinaný stedisko transplantací — KST, Czech Republic
- Lithuanian National Transplantation Bureau — NTB, Lithuania
- Univerzitna Nemocnica Martin — UNM, Slovakia
- Medical University Of Warsaw — MUW, Poland
- Országos Vérellátó Szolgálat — HNBTS, Hungary
- Paraskevaïdion Surgical and Transplant Center of Cyprus — PSTC (until 31 December 2010), Cyprus
- Pauls Stradins Clinical University Hospital, Latvian Transplantation Centre — PSCUH, Latvia
- Polish Transplant Coordinating Centre — POLTRANSPLANT, Poland

### EU contribution

This project has received co-funding from the European Union in the framework of the **Health Programme 2008–2013** (Grant: 20091103).

## 2<sup>ND</sup> Conference on Organ Transplantation: Ethical, Legal and Psychosocial Aspects — Expanding the European Platform (ELPAT)

*This project has received co-funding from the European Union in the framework of the Health Programme 2008–2013 (Grant: 20094102).*

The general objective of the conference was to expand the Ethical, Legal and Psychosocial Aspects of organ Transplantation (ELPAT) platform towards the new EU Member States, candidate countries and other eastern European countries; and to foster improvement in donation policies and practices. The conference holder was the European Society for Organ Transplantation.

Specifically, the conference aimed to provide an opportunity to increase ELPAT members from eastern European countries and their participation in study projects, gaining insight in the differences between national organ donation

policies and increasing knowledge and awareness of the problems faced in the area of donation and transplantation in EU Member States with a focus on the new MS.

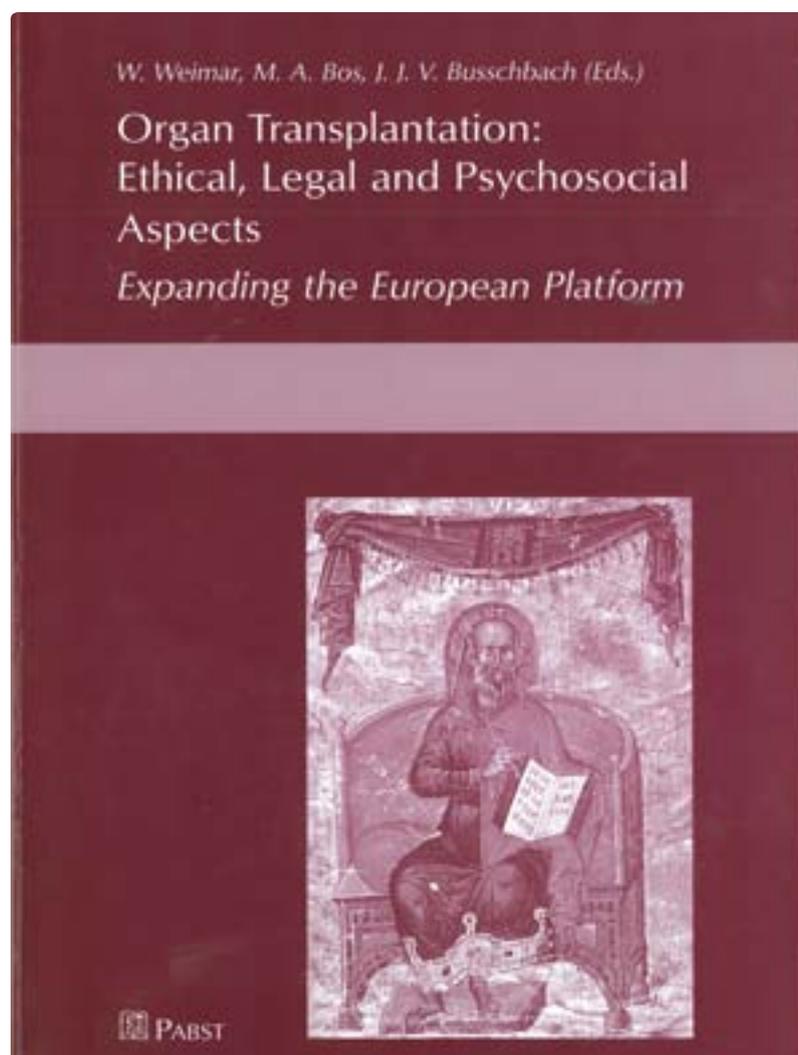
The conference ‘**Organ Transplantation: Ethical, Legal and Psychosocial Aspects — Expanding the European Platform**’ took place on 17–20 April 2010 in the World Trade Centre Rotterdam, the Netherlands.

*‘ELPAT attempts to be the movement from which research groups can structure their efforts by working together. Especially the rapid expansion of the European Union creates vast opportunities for cooperation between the various nations, although at the same time it may create problems that we have to face, e.g. equal access to healthcare,’* Prof. Willem Weimar, Chair, Professor of Internal Medicine at the Erasmus University Rotterdam, the Netherlands, welcomed the conference participants on behalf of the organising committee.

The conference addressed a wide range of different types of stakeholders such as medical scientists; experts in (bio-)ethics, law and psychology; medical practitioners in transplantation; students; public health professionals and health policymakers; civil society and international organisations.

**The overriding theme of the conference<sup>(167)</sup> was crossing borders in organ transplantation**

Topics during plenary and parallel sessions reflected the focus topics of the ELPAT Working Groups: organ tourism and paid donation; diverse populations; legal and ethical boundaries; deceased donation; psychological care for living donors and recipients; and Samaritan/unrelated donation. The Conference programme included plenary morning sessions, late-morning



Conference Proceedings Book, available through PABST publishers

<sup>(167)</sup> The Programme and abstract book of the Conference is available here: <http://www.esot.org/Meetings/PublicPlatform/MeetingPlatform.aspx?MeetingPlatformUI=6>

meet-the-expert sessions, free communications and afternoon workshops and discussions.

The interest in the conference was high as indicated by the total number of registrations and the higher than expected number of abstracts received prior to the conference. Altogether 297 people registered for the conference from 44 different countries: 30 European and 14 non-European. Due to the volcanic eruptions in Iceland, a total of 175 people managed to attend, out of which 162 people from 12 European countries.

### Successful expansion of the ELPAT platform and strengthened cooperation with new EU Member States

One of the main objectives of the conference was the expansion of the ELPAT platform to countries from eastern Europe. As a result of the conference, the ELPAT platform successfully expanded with about 23 new members from the new EU Member States and candidate countries.

Additionally, a new project was launched under the Seventh Framework Programme titled 'Living Organ Donation in Europe' (see page 208). Half of the participating partners in this project were from the new EU Member States and almost all of the project partners were involved in the ELPAT conference either as organiser, chair speaker or delegate.

As a further direct post-conference achievement, a follow-up expert working group meeting took place in October 2011 in Sofia, Bulgaria. The Bulgarian Centre for Bioethics invited ELPAT experts from 'old' EU Member States to share information and knowledge with the aim to improve donation and transplantation in Bulgaria. The contacts established for this meeting were a direct result from personal meetings at the 2<sup>nd</sup> ELPAT conference.

### Sharing experiences and knowledge for improved donation policies and practices in the future

The conference had contributed to the improvement of knowledge on the various ethical, legal and psychosocial aspects of donation and transplantation through its wide range of innovative topics presented in the scientific programme and through the participation internationally renowned experts during and after the conference.

“ELPAT attempts to be the movement from which research groups can structure their efforts by working together. Especially the rapid expansion of the European Union creates vast opportunities for cooperation between the various nations, although at the same time it may create problems that we have to face, e.g. equal access to healthcare.”

Prof. Willem Weimar

M. A. A. van Noord-Haubrich, F. J. E. E. Ambagtsheer, J. A. Kalvan Gestel, W. Zuidema, W. Weimar

## Volcanic Ash, Skype and the ELPAT Congress 2010\*

Marian A. A. van Noord-Haubrich, Frederike J. A. E. Ambagtsheer, Judith A. Kalvan Gestel, Willy Zuidema, Willem Weimar  
Erasmus Medical Center Rotterdam, Dept. of Internal Medicine – Kidney Transplantation, Rotterdam, The Netherlands



Figure 1 (REUTERS/Lucas Jackson)

### How Skype Saved the ELPAT Congress

#### Before the Congress

"News around the world on Thursday April 15<sup>th</sup>, 18:00 hours: In Iceland, the Eyjafjallajökull continues to billow smoke and ash. Therefore all flights in Northern Europe are cancelled." At this time over 300 doctors, ethicists, legal experts, psychologists, philosophers, and poli-

\* This congress was organized by ELPAT, the European platform on Ethical, Legal and Psychosocial Aspects of Organ Transplantation and ESCOT, the European Society for Organ Transplantation. The congress received funding from the European Commission and the Dutch Ministry of Health, Welfare and Sport.

16

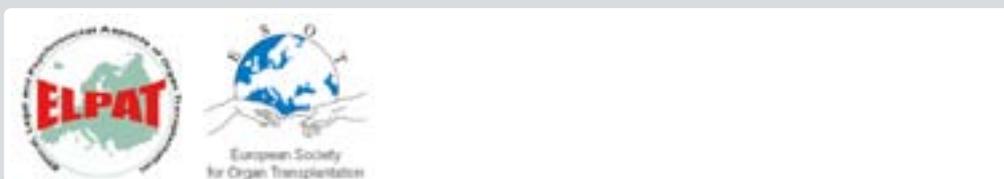
How Eyjafjallajökull endangered the conference

### ELPAT conference proceedings book

A book on the 2<sup>nd</sup> ELPAT Conference proceedings was compiled after the event with the aim to share novel information and increase knowledge in the field of ethical, legal and psychosocial aspects of organ transplantation. The book, entitled 'Organ Transplantation: Ethical, Legal and Psychosocial Aspects. Expanding the European Platform' (edited by W. Weimar, M.A. Bos and JJ Busschbach), was published by Pabst Science Publisher in 2011. It contains over 50 papers from conference participants on a range of subjects that dominated

contemporary policy and practice in the ethical, legal and psychological aspects of transplantation medicine.

All those who registered for the 2<sup>nd</sup> ELPAT Conference and first authors of the publication received a free copy of the book. Additionally, *'the publication of the book was announced through ELPAT/ESOT dissemination channels such as the ELPAT/ESOT Newsletter to around 9 000 transplant professionals in the world,'* explained Frederike Ambastsheer, ELPAT coordinator, at Erasmus University Rotterdam. The book can be ordered through the ELPAT website ([www.elpat.org](http://www.elpat.org)).



### Further information:

EAHC Project Database:

<http://ec.europa.eu/eahc/projects/database.html?prjno=20094102>

Conference booklet:

[http://www.esot.org/Files/Elpat/Content\\_Files/txmed\\_1-2007.pdf](http://www.esot.org/Files/Elpat/Content_Files/txmed_1-2007.pdf)

### Project team:

European Society for Organ Transplantation — ESOT

Hanzeplein 1

9713 GZ Groningen

NETHERLANDS

Tel. +31 642668336

Fax +31 104366372

### EU contribution

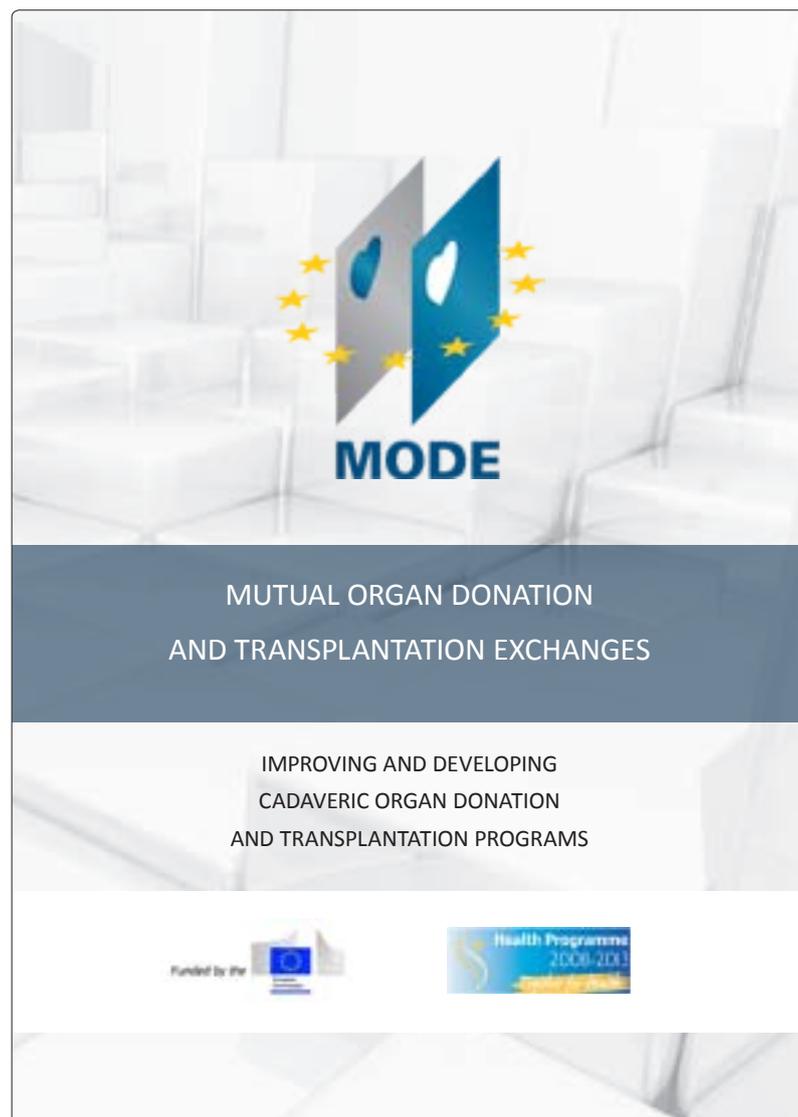
This project has received co-funding from the European Union in the framework of the **Health Programme 2008–2013** (Grant: 20094102).

## Joint Action on Mutual Organ Donation and Transplantation Exchanges: Improving and developing deceased organ donation and transplantation programmes (MODE)

*This joint action has received co-funding from the European Union in the framework of the **Health Programme 2008–2013** (Grant: 20102101).*

*“The preparatory phase was an opportunity for all partner countries to analyse the organisational situations of donation and transplantation in their respective country from the point of view of the implementation of Directive 53/2010.”*

*Dr Alessandro Nanni Costa, scientific leader of the project (Italian National Transplant Centre)*



*The final brochure summarising the results of MODE Joint Action*

Eleven partners, the majority of them from the new EU Member States, have worked together to implement MODE between January 2011 and June 2012. The project was coordinated by the Italian National Transplant Centre.

The main objective of MODE was to promote the transfer of best practices in the field of deceased organ donation and transplantation in light of the implementation of Directive 2010/53/EC on quality and safety of human organs. It aimed to facilitate the creation of positive synergies among participating Member States to support decision-making.

Paola Di Ciaccio, project manager, at the Italian National Transplant Centre, explains the main concepts of MODE: *‘Organ donation and transplantation have different practices and different levels in the countries of Europe. Sharing knowledge and skills in selected fields of interest could be an incentive to overall progress in organ donation and transplantation.’*

The MODE partners have identified best practices in deceased organ donation and transplantation. Based on their findings they facilitated the sharing of best practices via organising on-site visits in five countries and they provided specialised trainings.

### Identifying best practices in deceased organ donation

The MODE partners self-assessed their respective national donation and transplantation systems in a SWOT analysis with respect to the implementation of the Action Plan on Organ Donation and Transplantation (2009–2015). The project also mapped the interests and training needs of partners. Three priority action areas were finally selected for the purposes of best practice sharing: promoting quality programmes to improve organ donation; organisational models for donation and transplantation; and evaluation of post-transplantation results.

Dr Alessandro Nanni Costa, scientific leader of the project (Italian National Transplant Centre) (MODE White Paper)<sup>(168)</sup>, explains the added value of MODE: ‘The preparatory phase was an opportunity for all partner countries to analyse the organisational situations of donation and transplantation in their respective country from the point of view of the implementation of Directive 53/2010.’

Using the findings of the assessments, MODE partners have developed and organised best practice transfer activities, namely the five on-site visits and a set of specialised short- and/or medium-term training courses.

### On-site visits to facilitate best-practice transfer

Altogether five on-site visits took place during the MODE project. The visits were structured in a way that gave an opportunity to the hosting partners to present their organ donation and transplantation systems and discuss some specific practical areas in more detail. After each on-site event, the visiting partners evaluated the programme and the implementation potentials of the presented best practices with respect to their own countries.

These on-site visits were considered as important initial points for future bi- or multi-lateral cooperation among those partner countries and organisations who in the future wished to improve their donation practices through

“Organ donation and transplantation have different practices and different levels in the countries of Europe. Sharing knowledge and skills in selected fields of interest could be an incentive to overall progress in organ donation and transplantation.”

Paola Di Ciaccio, project manager,  
Italian National Transplant Centre

adapting best practices in their national contexts and health systems.

### Specific trainings to promote best-practice transfer

The training topics were linked to the topics that were selected for the on-site visits, so that all project efforts aiming at the transfer of best practices were more effective and focused on well-defined items. Based on the training needs assessment and on the experiences of the on-site visits, the following Action Plan priority areas were selected for the specialised training courses:

- traceability and bio-vigilance in organ transplantation, analysing how organisations perform in Europe and in

### MODE on-site visits and the presented best practices

Date	Hosting partner	Action plan goal	Priority action	Best practice
7 June 2011	ONT Spain	Increasing organ availability	Quality improvement programmes	Quality improvement, quality management, safety management
9 June 2011	KST Czech Rep.	Enhancing efficiency and availability of transplantation (TX) systems	Supporting and guiding organisational models	Protection against transmissible and neoplastic diseases, traceability
20 June 2011	ASST Portugal	Enhancing efficiency and availability of TX systems	Supporting international exchange of organs for transplantations	Interchange of organs between Member States
7 July 2011	ST Slovenia	Enhancing efficiency and availability of TX systems	Increasing deceased donation to their full potential	Multi-organ donors, international organ exchange
12 July 2011	CNT Italy	Improving quality and safety of TX	Evaluation of post-transplantation results	Accreditation of TX centres, evaluation and auditing of TX results

Source: MODE White Paper, 2012.

<sup>(168)</sup> MODE White Paper is available on the project website: [www.mode-ja.org](http://www.mode-ja.org)

other developed countries, and what tools can be useful to implement to comply with the mandate of Directive 2010/45/EU on standards of quality and safety of human organs intended for transplantation;

- quality assurance in the donation process as a means to evaluate the potential for organ donation and standardise the procedures and guidelines for improving the donation of organs from brain death donors;
- accreditation of transplant centres and how to improve safety and quality in the allocation of organs and evaluation the outcomes of the transplantation process.

The specialised courses started with an e-learning session that took place between 27 April and 3 May 2012. This was followed by three 1-day face-to-face training courses in Spain, organised by the Organización Nacional de Trasplantes. The faculty of the training courses were experts who had European project experience related to the Action Plan in the selected fields.

## The day-to-day sessions and their focus areas

*7 May 2012: Reporting on adverse events and reactions*

Altogether 20 people (staff from national organisations/competent authorities) participated from eight countries.

*8 May 2012: The Quality Assurance Programme of the Donation Process in Spain: Key Factors to Improve (Workshop)*

Eighteen competent authority staff or their appointed national experts took part in this workshop from nine different countries.

*9 May 2012: Quality assurance of the transplantation process*

Altogether, 18 people participated from eight different countries on this specialised training course.



## Information about the project and its results

Information about the project and its results were drawn up in a final document called the **MODE White Paper**. This document is publicly available on the project website: [www.mode-ja.org](http://www.mode-ja.org). The project has also published a Layman Brochure that summarises the main aspects of the MODE joint action ([www.mode-ja.org](http://www.mode-ja.org)). Five hundred copies of this brochure have been distributed in different events by partners. National authorities and policymakers have been informed about the activities and results of MODE in two competent authority meetings in 2011 and at the High-Level Conference — EU Health Programmes: results and perspectives, organised by the European Commission on 3 May 2012. A wide range of target groups were reached through international events: 24 presentations in four countries provided opportunity to present and discuss the status and results of the projects.

*'The innovative aspect of the project was, however, to allow partners to highlight their fields of interest through an analysis of strengths and weaknesses and to specify their training needs*

*“Due to the complexity of the process and the variables in the organisational situations, each country has something to “offer” and much to learn from others. In our action such comparison has always been constructive, allowing the knowledge and understanding of “different worlds” and the acquisition of new skills that, maybe, cannot be imported tout court, but are however a great stimulus for our mutual growth.”*

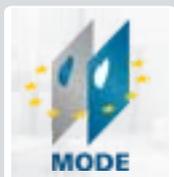
*Dr Nanni Costa about the MODE Joint Action*

*in those specific fields,' concludes Dr Alessandro Nanni Costa, scientific leader of the project (Italian National Transplant Centre).*

*'MODE will also provide useful inputs to and have its ideal continuation in the ongoing ACCORD joint action that is planning to implement twinning arrangements for best practice sharing in selected countries,' concludes Paola Di Ciaccio, project manager.*



*Kick-off meeting of the Joint Action MODE*



### Further information:

EAHC Project Database:

<http://ec.europa.eu/eahc/projects/database.html?prjno=20102101>

Project website

<http://www.mode-ja.org>

### Project team:

Centro Nazionale Trapianti, Istituto Superiore di Sanità  
 Viale Regina Elena, 299  
 00161 Rome RM  
 ITALY  
 Tel. +39 0649904040  
 Fax +39 0649904101  
 E-mail: [centronazionale.trapianti@iss.it](mailto:centronazionale.trapianti@iss.it)

### Associated partners:

- Autoridade para os Serviços de Sangue e da Transplantação, Portugal
- Bulgarian Executive Agency for Transplantation (BEAT), Bulgaria
- Department of Health of Malta, Malta
- Institute for Transplantation of organs and tissues of the Republic of Slovenia — Slovenija Transplant, Slovenia
- Koordinaní stedisko transplantací, Czech Republic
- National Transplant Bureau, Lithuania
- Organizacion Nacional de Trasplantes, Spain
- Országos Vérellátó Szolgálat, Hungary
- Pauls Stradins Clinical University Hospital, Latvia
- Tartu University Hospital, Estonia

### EU contribution

This joint action has received co-funding from the European Union in the framework of the **Health Programme 2008–2013** (Grant: 20102101).

## Achieving Comprehensive Coordination in Organ Donation throughout the European Union (Joint Action ACCORD)

*This joint action has received co-funding from the European Union in the framework of the Health Programme 2008–2013 (Grant: 20102101).*

In order to improve the situation of substantial heterogeneity among the European countries in donation and transplantation activities, a consortium of 23 national transplantation authorities and 10 collaborative partners, mostly major international organisations, have joined their efforts to implement the ACCORD Joint Action.

ACCORD — ‘Achieving Comprehensive Coordination in Organ Donation throughout the European Union’ — is co-funded by the European Commission under the Health Programme (2008–2013). The project is initiated and coordinated by the Spanish National Transplant Organisation (ONT) and started in May 2012 with the kick-off meeting in Madrid. The project is expected to run until November 2015.

The general objective of ACCORD is to strengthen the full potentials of EU Member States in the field of organ donation and transplantation and to improve cooperation between them. Therefore, this Joint Action is a further necessary

step to assist EU Member States for a consistent implementation of Directive 2010/53/EU of the European Parliament and of the Council of 7 July 2010 on standards of quality and safety of human organs intended for transplantation and the Action Plan on Organ Donation and Transplantation (2009–2015): Strengthened Cooperation between Member States.

The countries participating in the Joint Action ACCORD have identified six specific objectives as currently most vital to work on during this project. These are:

- improving Member States’ information systems on live organ donation;
- improving the deceased donation process in the EU countries through describing the most common pathways applied to patients with devastating brain injury and their impact on the potential of donation;



The relation of the Joint Action ACCORD to Directive 2010/53/EU and Action Plan ([www.accord-ja.eu](http://www.accord-ja.eu))

- improving end-of-life management in a way to promote donation through developing a rapid improvement toolkit adapted to the identified end-of-life care models;
- providing concrete assistance through collaborations and trainings between EU Member States in specific areas related to Directive 2010/53/EU and the Action Plan on Organ Donation and Transplantation;
- providing useful insights and recommendations for future twinning initiatives; and
- disseminating and rendering sustainable the results and outputs of the project.

The Joint Action ACCORD has organised its work in three work packages focusing on three specific fields and activities.

### Living donor registries

Live donation is an important source of organs. As living donors are facing evident risks it is paramount to ensure that living donors receive

appropriate and comprehensive care (live donor care) that is in compliance with universal medical, ethical and psychosocial standards throughout Europe. Living donor registries are an essential component of such appropriate and comprehensive care and increase the safety of living donation.

The aims of this work package are to improve information systems on live organ donation through the provision of recommendations for designing and managing structured live donor registries and through setting down a model for supranational data sharing ('registry of registries').

The institutions that are working in this work package will review and analyse existing live donor registries in partner countries and produce a comprehensive state-of-the-art overview. This expert review and analysis shall form the basis for recommendations about the necessary governing rules as well as minimum requirements of data sets of future registries. Additionally, the feasibility of setting up a European live donor registry is planned to be piloted among those partner countries that already have established registration systems.

The screenshot shows the ACCORD website homepage. At the top, there is a blue navigation bar with the ACCORD logo on the left and links for 'Contact' and 'Member Access' on the right. Below the navigation bar, there is a horizontal menu with links for 'ACCORD', 'PARTICIPATING PARTNERS', 'WORK PACKAGES', 'PROJECT EVOLUTION', 'NEWS AND EVENTS', and 'FAQS'. The main content area features a large image of three surgeons in blue scrubs and masks, focused on a surgical procedure under a bright light. To the left of this image is a text box titled 'What is ACCORD?' which provides a brief overview of the project. Below the main image, there are two columns of text: 'Events and Documents' and 'Links'. The 'Events and Documents' section lists a 'Kick-off Meeting' held on 31st May 2012 in Madrid, Spain, and provides details about the location and program. The 'Links' section includes links to the 'European Commission Projects database' and the 'European Commission DG Health and Consumers' website. At the bottom of the page, there is a footer with copyright information and additional links.

The website of the Joint Action ACCORD ([www.accord-ja.eu](http://www.accord-ja.eu))

The final set of recommendations for developing a live donor registry and a common European registry will aid EU Member States, particularly those who are without a functioning live registry, in the set-up and design of European-wide coordinated registries. It will also facilitate international data sharing and provide comparable information in the area of live donors available for improved services in Europe. These activities will not only contribute to a safer live donor care in Europe, but also will increase coherence to existing regulations in this field.

### Cooperation between intensive care units and donor transplant coordination

Many factors influence the organ donation rate, such as the way that possible donors are being identified in the hospital setting, or how effectively the clinical decision-making process is organised in the hospital's end-of-life practices (e.g. intensive care units). These end-of-life practices are organised in different ways across hospitals, regions and countries in Europe. This varying organisation leads also to the variation in deceased donation rates among countries.

The second technical work package of the Joint Action ACCORD therefore works on increasing the availability of organs from deceased donors by strengthening the cooperation between intensive care units and the donor transplant coordinators. In focusing on the potential role of end-of-life care pathways in the deceased donation process, this work package is analysing end-of-life practices and clinical decision-making processes in the participating Member States and is exploring their impact on the potential and actual donor pool. The critical goal is to identify areas for improvement.

A clinical reference group will review the variations in end-of-life care pathways for patients with brain injury in a selected sample of hospitals. In this area, the project team is using a benchmarking approach, which is an effective way to identify improvements in the process of when and how a possible donor is becoming an actual donor. The work shall guide the building of an effective connection between intensive care units and donor transplant coordinators, which in turn increases available organs derived from deceased donation. A set of recommendations and a toolkit methodology to improve the

“*Very sensitive changes are taking place in the management of critical care patients at the end of life ... and it is not to describe how to make the process, but what is the point(s) considered the key for success ...*”

*Rafael Matesanz, Director, Organizacion Nacional de Trasplantes, Coordinator of ACCORD at the kick-off meeting of ACCORD on 31 May 2012 in Madrid, Spain*

end-of-life care pathways in order to promote and optimise the deceased organ donation processes will be the output of this work.

### Twinning programmes on organ donation and transplantation

Direct exchange of specific national experience can effectively meet the needs of other countries. Twinning activities further promote that specific knowledge acquired in one country is transferred and implemented in others hospitals, regions and countries.

Therefore, the third technical work package of the Joint Action ACCORD is working on organising the exchange of best practices and consolidated expertise and tools through specific twinning programmes. The topics and specific areas which these twinning programmes focus on are either topics covered by Directive 2010/53/EU or topics recommended by the Action Plan on organ donation and transplantation. Building on the twinning experiences not only from this work package, but also from past twinning experiences, this work package will also provide recommendations for future twinning initiatives in the field of organ donation and transplantation.

The institutions participating in this work package of the Joint Action ACCORD are planning and organising the following twinning programmes with detailed protocols:

- the organisation of the national procurement system, the data collection and analysis as well as support of paediatric kidney transplantations is addressed to Bulgaria with the support of France;
- setting up a national accreditation system for transplant centres is addressed to

Cyprus, the Czech Republic, Malta and Lithuania with the support of Italy;

- the testing of a training platform in organ recovery for surgeons will be performed in Hungary with the support of the Netherlands.

The experiences gained in these three twinning projects will allow setting up a potential European Union tool for the accreditation of transplant centres, training in organ recovery and one-to-one support for the development of transplant systems. This work package also develops a guideline for further twinning initiatives in the field.

### Expected outcome and its added value

The expectations towards the Joint Action ACCORD as a whole are to help in the consistent implementation of Directive 2010/53/EU of the European Parliament and of the Council of 7 July 2010 on standards of quality and safety of human organs intended for transplantation across the European Member States, and to provide concrete assistance in meeting the objectives of the Action Plan.

It represents a strategic opportunity in time as the national provisions of the recent Directive are being worded and ACCORD can support the alignment of such provisions and procedures, which overall shall lead to a safe and high-quality organ donation and transplantation process with the ultimate and concrete goals of

<p><b>WP4</b></p> <p><b>MAPPING</b> The action will perform a state-of-art on existing living donor registries in partner countries.</p> <p><b>SHARING</b> A living donor registry of European living donor registries is one final goal of this ACCORD core Work package .</p> <p><b>BUILDING</b> Putting expertise in common and defining clinical parameters for building up a living donor registry will be discussed and agreed. Living donor registries are essential components of national strategies targeted to increase the safety of living donation in the European Union.</p>	<p><b>WP4</b></p> <p><b>LIVING DONOR REGISTRIES</b></p> <p><i>WP leader: Dutch Transplant Foundation</i></p>
<p><b>WP5</b></p> <p><b>MAPPING</b> A review of existing end-of-life care pathways in different Member States will be carried out, with special focus on practices relevant to organ donation.</p> <p><b>SHARING</b> Best practices for facilitating the identification of potential donors and their conversion into actual donors will be shared, to guide on the establishment of an effective connection between intensive care units and donor transplant coordinators that facilitates deceased donation.</p> <p><b>BUILDING</b> New tailored-to local needs tools that will allow Member States to improve performance in the donation process and to increase the number of deceased donors will be supplied.</p>	<p><b>WP5</b></p> <p><b>COOPERATION BETWEEN ICU PROFESSIONALS AND DTCS</b></p> <p><i>WP leader: National Health Service Blood and Transplant</i></p>
<p><b>WP6</b></p> <p><b>MAPPING</b> Expertise of a given Member State can meet the needs of others. Three twinning programmes will be performed in ACCORD with the final aim of improving performance, quality and safety of the supported countries' transplant systems.</p> <p><b>SHARING</b> The organization of the national procurement system, data collection and analysis and the support of kidney paediatric transplantations will be addressed in Bulgaria. Setting up a national accreditation system for transplant centres will be the area covered in Cyprus, Czech Republic, Malta and Lithuania testing a training platform in organ recovery for surgeons will be covered by the cooperation with Hungary.</p> <p><b>BUILDING</b> Setting up potential EU tools for the accreditation of Transplant Centres, training in organ recovery, and one-to-one support for the development of a Transplant system will be addressed by capitalizing on experience. Guideline for further Twinning models in the field is another goal of this ACCORD work package.</p>	<p><b>WP6</b></p> <p><b>TWINNING</b></p> <p><i>WP leader: Agence de la biomédecine</i></p>

The brochure ACCORD — A unique opportunity in time ([www.accord-ja.eu](http://www.accord-ja.eu)).

saving the lives of those patients, which are in urgent need of an organ transplant, wherever in Europe. This context also sets the subtitle of the project 'ACCORD — a unique opportunity in time'.

Moreover, the project introduces elements of innovation in the field of donation and transplantation, for instance, in the form of a European-wide common foundation for the development of live donor registries, in the form of a unique description on the different approaches to end-of-life practices and a tailored model to optimise the realisation of the deceased donation process, and in the form of a guidance approach for future twinning initiatives.

The main target groups of the project are national and regional institutions, which are involved in organising and setting the political framework of organ donation and transplantation in respective EU Member States. Further target groups are professionals, patient associations and the public.

“Every country should make a diagnosis of the situation and find the most adequate way towards self-sufficiency; there is not a single way to self-sufficiency, well-proven successful models should be taken as reference ...”

*Rafael Matesanz, Director, Organizacion Nacional de Trasplantes, Coordinator of ACCORD at the kick-off meeting of ACCORD on 31 May 2012 in Madrid, Spain*

To ensure that the project's approach, strategy, results and outputs are accessible to all target groups, the project has: produced a layman brochure; is issuing regular newsletters for disseminating progress and results; will organise a final dissemination event at the end of the Joint Action project; and will maintain a close link with the World Health Organisation and the Council of Europe to ensure that the results of the project are made available also outside the European Union. The project website is already available at the following link: [www.accord-ja.eu](http://www.accord-ja.eu).



*Pilar Farjas, General Secretary of the Spanish Ministry of Health, Social Services and Equity, and Rafael Matesanz, Director of the Spanish National Organisation for Organ Transplantation (ONT), open the ACCORD Joint Action on 31 May 2012 in Madrid, Spain*



### Further information:

EAHC Project Database:

<http://ec.europa.eu/eahc/projects/database.html?prjno=20112102>

Project website

<http://www.accord-ja.eu/>

### Project team:

Organización Nacional de Trasplantes (ONT)

C/ Sinesio Delgado, 6-8

PO-BOX

28029 Madrid

SPAIN

Tel. +34 902300224

Fax +34 902300226

E-mail: <http://www.accord-ja.eu/contact>

### Associated partners:

- Agence de la Biomédecine — ABM, France
- Autoridade para os Serviços de Sangue e da Transplantação, ASST, Portugal
- Deutsche Stiftung Organtransplantation — DSO, Germany
- Helsedirektoratet — HDIR, Norway
- Dutch Transplantation Foundation — DTF, Netherlands
- Executive Agency for Transplantation — BEAT, Bulgaria
- Feidhmeannacht na Seirbhíse Sláinte — HSE, Ireland
- Hellenic Transplant Organisation — HTO, Greece
- Zavod Republike Slovenije za presaditve organov in tkiv Slovenija Transplant, Slovenia
- Istituto Superiore Di Sanità — ISS, Italy
- Koordinační středisko transplantací — KST, Czech Republic
- Ministry for Social Policy, Health, the Elderly and Community Care — MHEC, Malta
- Ministry of Health of the Republic of Cyprus — MOH CY, Cyprus
- Ministarstvo zdravlja Republika Hrvatska — MOHSW, Croatia
- Agenția Națională de Transplant — ANT, Romania
- Nacionalinis transplantacijos biuras — NTB, Lithuania
- National Health Service Blood and Transplant — NHSBT, United Kingdom
- Országos Vérellátó Szolgálat — HNBTS, Hungary
- Paula Stradiņa Klīniskā universitātes slimnīca — PSCUH, Latvia
- Sihtasutus Tartu Ülikooli Kliinikum — TUH, Estonia
- Národná transplantacná organizácia — NTO, Slovakia
- Centrum Organizacyjno-Koordynacyjne ds. Transplantacji 'Poltransplant', Poland

### EU contribution

This joint action has received co-funding from the European Union in the framework of the **Health Programme 2008–2013** (Grant: 20112102).

## European Training Course for Trainers in Transplant Donor Coordination in the European Union

*This training course has been funded by the European Union in the framework of the Health Programme 2008–2013 (Service Contract: 20106102).*

In 2011, DG SANCO of the European Commission provided teacher training to a total of 79 healthcare professionals from 24 EU Member States (all of them experts in the donation and transplant process) in order to promote the figure of 'Transplant Coordinator', which is a key success factor of the internationally recognised Spanish donation and transplantation model — one that has given such good results year after year in Spain.

This course addressed part of the Priority Action Number 1 of the European Action Plan on Organ Donation and Transplantation (2009–2015) which is the '*Promotion of the role of transplant donor coordinators in every hospital where there is potential for organ donation*'. It was funded by the European Union under the EU Health Programme in the framework of a service contract.

The course was developed in Spain, designed and executed by the IAVANTE Foundation, an organisation based in Granada/Spain and specialised in healthcare training, in collaboration with the Spanish National Transplant Organisation (ONT).

### The Spanish donation and transplantation model

The extraordinary performance of the transplant coordinators, along with the excellent organisational system and the generosity of the citizens, have permitted Spain to beat its own record for donation and transplantation in 2011 with a total of 1 667 donors allowing a total of 4 218 transplants to be performed. This represents an increase of 11.8 % compared with the previous years, and a further 445 patients transplanted. These figures are ground-breaking, both in absolute figures as well as in relation to the number of inhabitants, which has raised the donation rate to 35.3 donors per million population (donation rate in the European countries was 18.7 donors per million population in 2010). It should also be noted that the rate of refusal by family members to donate has fallen by 4 points and was 15 % in 2011. Once again this represents

Spain's leadership in donation and transplantation and its capacity for continuing improvement.

### Objectives of the Training Course for Trainers in transplant donor coordination in the European Union

DG SANCO of the European Commission financed this training course through a public call for tenders; the design and running of the course was the result of collaboration between the IAVANTE Foundation with the Spanish National Transplant Organisation (ONT). The training programme was based on the consortium's wide experience in this field and in healthcare training using simulation techniques. It followed the course model that the ONT and the IAVANTE Foundation have been running since 2006 in the CMAT Medical Simulation Centre, Granada, in which more than 240 healthcare professionals from Spain and Latin America have been trained to date, with a satisfaction rate of 93 %.



Course announcement  
for the training course  
(<http://www.etc.iavante.es/>)



Training in the Intensive Care Unit Simulation Theatre of the IAVANTE CMAT foundation



*Simulation methodologies involved the use of advanced robotic simulators of the IAVANTE CMAT foundation, which react to the medicines administered*

The training programme was designed within the framework of the European Directive on Quality and Safety of Organs for Transplantation and was based on the Spanish model of donation and transplantation. In this organisational model of the process of donation and transplantation, the coordinator is the figure responsible for the detection of possible donors, as well as the care of the relatives of the donor and for the communication needed to obtain authorisation for the donation. The transplant coordinator is also the healthcare professional responsible for preparing the complex transplant process logistics between different hospitals as well as the management of waiting lists and donation promotion. The terms 'transplant coordinators', 'transplant donor coordinators' and 'key donation personnel' might cover different tasks, realities and organisational systems in the various EU Member States, but these key persons are all involved in activities covering the chain from organ donation to organ transplantation.

*“The best way to learn about these topics is making workshops, making a practice, because you can read about these topics in every book. But we make this practice with an actor, it is better than a mechanical robot, and they can see the reflexes, and we teach them about the pathological responses ... We can play any kind of situation that happens in real life.”*

*Diego Mora, Transplant Coordinator at the Juan Ramon Jimenez Hospital, Huelva, Spain*

### **The transplant coordinator is the healthcare professional responsible for preparing the complex transplant process logistics between hospitals**

Competent Authorities on organ donation and transplantation from the EU Member States selected the most suitable professionals in their respective countries to attend this training programme. The goal of this initiative is to train professionals in the EU to develop training courses in their respective countries or to integrate new elements into their existing training courses, in order to teach other professionals in all or part of the transplant coordination tasks, depending on each country's reality and needs. The final aim was to improve the results of the donation activity in Europe, thus increasing the possibility of transplantation for the citizens who need it.

### **Content of the programme**

The selection process was opened from December 2010 to February 2011. By the end of the deadline, 103 nominees had registered from 25 Member States. Finally, altogether 79 students attended the course: 41 students on the first course and 38 on the second. Twenty-five out of the then 27 Member States were represented on the course.

Two editions of the course took place between 5 September and 7 October as well as between 24 October and 25 November 2011. Each edition of the course consisted of an initial e-learning phase of 10 days, followed by face-to-face training with theoretical lessons and practical workshops of 5 days, ending with a post-course assignment of 10 days, where the students had to design a training course for coordinators taking into account the reality and needs of their own countries. The face-to-face phases of the two courses were held at the IAVANTE CMAT medical simulation centre in Granada (Spain), which is managed by the Andalusian Regional Health Ministry. For the online part of the course a tailor-made e-learning platform was designed to facilitate communication among all participants and to access content materials.

The participants reviewed the different phases of the donation process from a didactic perspective, ranging from the detection of potential donors to the maintenance of the vital signs of the donor until organ extraction as

well as the family interview in which donation consent is requested. There was specific training in didactic methodologies and also a review of the legal and ethical framework applicable in the EU setting. These activities were carried out using the simulated scenarios in CMAT which include critical care units and consultation rooms, providing the coordinators with high-fidelity simulated scenarios to recreate realistic work environments. Workshops were also included using role-play as well as simulation methodologies involving the use of advanced robotic simulators which react to the medicines administered.

During the course, the participants were trained in the necessary knowledge, materials and didactic methodology so that, on returning to their respective countries, they would be able to adapt what they learned in order to set up coordinator training courses according to their local requirements. As participants had different profiles and fields of expertise (including deceased donation/living donation, national/regional/local coordinators, intensivists, nephrologists and nurses), they could also highly benefit from the exchanges within the group, with the speakers and during the workshops.

The courses consisted of eight blocks:

“ *There is always something to learn, in this case making the comparison with other countries with different options and legislation, and also different possibilities for carrying out donor transplant surgery.* ”

*Daniela Maretti, Regional Transplant Coordinator, Lombardy, Italy*

- Unit 1: Donor identification, selection and evaluation
- Unit 2: Diagnosis of brain death
- Unit 3: Donor maintenance
- Unit 4: Retrieval and distribution of organs
- Unit 5: Non-beating heart donation
- Unit 6: Communication skills and relating to the family
- Unit 7: Ethics, legislation and organisational models. The role of coordinator
- Unit 8: Introduction to teaching methodology and skills



*'Passing the worst message ...' — Trainers for Transplant Donor Coordination train the interaction with relatives of deceased donors, which in this simulation are being played by professional actors*

### Results of the training course

A total number of 79 health professionals involved in donation and transplantation activities from 24 EU countries have been trained to train transplant coordinators in their respective countries. The average level of satisfaction of the participants for each of the courses was respectively 8.1 and 9 of a maximum of 10 points, which has demonstrated the overall high degree of quality in the courses, including scientific and organisational aspects.

*“The ultimate goal of the project was to increase the quality and quantity of donation and transplant coordination in the EU through training transplant coordinators to be able to go back to their countries and in turn train professionals there ... From the train-the-trainer approach we expected a multiplied effect with which we could increase the impact.”*

*David Riley, project manager, IAVANTE Foundation*

One month after completing the course, an impact assessment on the two courses was conducted through a post-course

self-assessment survey for all course participants, asking questions on transference of knowledge and impact. In this assessment, the indicator of ‘impact’ was defined as putting into practice the knowledge acquired during the course, i.e. the planning, designing and implementing of training courses for transplant coordinators in the respective regions of the course participants. According to David Riley, ‘70 % of Member States responded; the majority of course participants were directly applying the knowledge gained during the course for training in their countries, either by setting up new training or improving the existing ones using the knowledge gained in the course.’

‘Many participants pointed out in their course evaluation that the course gave them a unique opportunity to come together to share and exchange knowledge in transplantation coordination from all over Europe,’ explained Mr Riley. Participants also emphasised that meeting other professionals and knowing how transplants are coordinated in other countries was very useful. ‘It opts towards making transplant coordination on a European level a reality which can have an enormous impact on the health of European citizens.’

This course can be seen as a role model in mutual learning among EU Member States.



### Further information:

Project website  
<http://www.etc.iavante.es/>

### Project consortium:

CMAT, Advanced Multifunctional Centre for Simulation and Technological Innovation  
Iavante Centre in Granada Parque Tecnológico de Ciencias de la Salud  
Avda. de las Ciencias s/n  
18 100 Armilla (Granada)  
SPAIN  
Tel. +34 958002250  
E-mail: [formacion.gr@iavante.es](mailto:formacion.gr@iavante.es)  
Webpage: <http://www.iavante.es>

### Consortium partners:

- Organización Nacional de Trasplantes (ONT), Spain
- Spanish Ministry of Health, Madrid, Spain

### EU contribution

This training course has been funded by the European Union in the framework of the **Health Programme 2008–2013** (Service Contract: 20106102).

# Study on the set-up of organ donation and transplantation in the EU Member States, uptake and impact of the EU Action Plan on Organ Donation and Transplantation (2009–2015)

*This study has been funded by the European Union in the framework of the EU Health Programme 2008–2013 (Service Contract: 20116141).*

The study on the set-up of organ donation and transplantation in the EU Member States, uptake and impact of the EU Action Plan on Organ Donation and Transplantation (2009–2015) is financed by the European Union under a service contract and carried out by the Netherlands Institute for Health Services Research (NIVEL). The implementation of the study started on 1 January 2012 and finished in February 2013.

Organ shortages are observed in all Member States and form an acute problem for patients in urgent need of an organ transplant. Since the early 1990s the European Union has recognised organ shortages as a subject that necessitates joint efforts from European Member States and the European Commission. In 2007 the Commission adopted a Communication to the European Parliament on organ donation and transplantation outlining a set of actions. This was followed by an Impact Assessment identifying major policy challenges for organ donation and

transplantation in Europe. In December 2008, the Commission adopted an Action Plan and a proposal for a Directive.

The Action Plan on Organ donation and transplantation (2009–2015) is a non-binding instrument that has been established in accordance with Article 168(2) and (4) of the Treaty on the Functioning of the European Union (TFEU) to help the Member States address three main challenges: the shortage of organ donations and the increase organ availability (Challenge 1 of the Action Plan), to make transplant systems efficient and accessible (Challenge 2) as well as to ensure quality and safety of donation and transplant procedures (Challenge 3). The Action Plan identifies 10 priority actions, most of them being supported by several actions.

The ACTOR study, conducted over the year 2012, is a mid-term research on the uptake and impact of the Action Plan (2009–2015). It results in a comprehensive analysis and overview of the organisation of organ donation and transplantation systems in every European Member State as well as at EU level. It will also provide an in-depth review of the implementation of the Action Plan in Member States with recommendations for further steps to be taken.

The study will consist of a systematic analysis of the available scientific and non-scientific literature on each of the 10 priority actions and its implementation. This data will be supplemented, corrected and contextualised through the consultation of Competent Authorities in the Member States and European institutions, through structured questionnaires and the use of an online database. Existing indicators or data will be evaluated and supplemented so that strengths, weaknesses, opportunities and threats of and for the implementation of the Action Plan can be determined. Based on this analysis, Member State specific, 'priority action'-specific and general recommendations for the second-half period of the Action Plan implementation can be formulated.

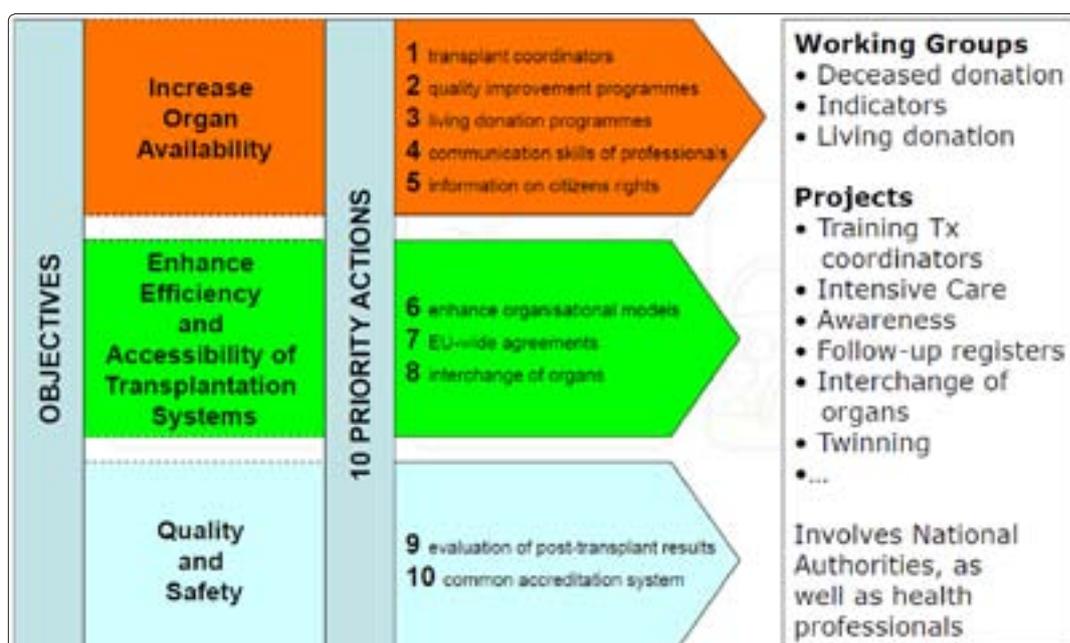


### Expected outputs of the ACTOR study

Two major outputs are expected from this study: firstly, a comprehensive overview of the organisation of organ donation and transplantation systems in every EU Member State as well as at EU level, providing a general picture as well as detailed elements for each of the priority actions of the Action Plan; and secondly, an in-depth assessment of the implementation of the Action Plan in Member States with recommendations for further implementation, based on the analysis of strengths, weaknesses, opportunities and threats (SWOT analysis).

The activities of the study consisted of four major steps. The research group started with an assessment of organ donation and transplantation activities in each of the European Member States, including the general set-up and organisation at central and hospital level. This includes a description of background information on organ donation and transplantation activities through defining background indicators. A detailed description of the organ donation and transplantation system in each of the EU Member States and Croatia, Iceland, Liechtenstein, Norway, the former Yugoslav Republic of Macedonia, Montenegro, Switzerland and Turkey is the expected result from this work.

Priority Action 1	Promote the role of transplant donor coordinators in every hospital where there is potential for organ donation. Design indicators to monitor this action
Priority Action 2	Promote Quality Improvement Programmes in every hospital where there is potential for organ donation
Priority Action 3	Exchange of best practices on living donation programmes among EU Member States: Support registers of living donors
Priority Action 4	Improve the knowledge and communication skills of health professionals and patient support groups on organ transplantation
Priority Action 5	Facilitate the identification of organ donors across Europe and cross-border donation in Europe
Priority Action 6	Enhancing the organisational models of organ donation and transplantation in the EU Member States
Priority Action 7	Promote EU-wide agreements on aspects of transplantation medicine
Priority Action 8	Facilitate the interchange of organs between national authorities
Priority Action 9	Evaluation of post-transplant results
Priority Action 10	Promote a common accreditation system for organ donation/procurement and transplantation programs



The 10 priority actions of the Action Plan on Organ Donation and Transplantation (2009–2015): Strengthened cooperation between Member States ([http://ec.europa.eu/health/archive/ph\\_threats/human\\_substance/oc\\_organ/docs/organs\\_action\\_en.pdf](http://ec.europa.eu/health/archive/ph_threats/human_substance/oc_organ/docs/organs_action_en.pdf))

Thereafter, an assessment of the state of implementation for the 10 priority actions in each of the EU Member States has been carried out. As a result of this work, a state-specific mapping, analysis and assessment of the implementation process of the priority actions in each of the EU Member States is drawn up. The mapping analysis for the state of affairs of the implementation of the Action Plan shall be presented as a separate chapter in the final report.

Furthermore, an assessment of the engagement of Member States and the European Commission in common European-wide initiatives and projects as well as the outcome of these initiatives in relation to the 10 priority actions has been carried out. The focus of this work has been on searching, finding and organising all relevant project information. The study will furthermore include an overview and assessment of interaction of the Commission's Action Plan with other international initiatives undertaken by the WHO, the Council of Europe, Eurotransplant and Scandiatransplan and European professional organisations.

### The ACTOR survey/database

For the ACTOR study, NIVEL has developed a survey database. It is an online digital survey instrument with an option to upload PDF documents, which makes it a unique research tool. It shall also leave room for both researchers and Competent Authorities to comment and react to the answers and data given.

The survey is first filled in by the NIVEL researchers, on the basis of the research team's initial data gathering stage. Competent Authorities can subsequently verify, add and change the answers to the questions and leave comments and documents to support their answers.

Finally, an assessment of strengths, weaknesses, opportunities and threats of and for the implementation of the Action Plan and recommendations for the second half-period of the Action Plan, both at EU and national level has been carried out and shall provide a summary of the complete study for each of the 10 priority areas. The analysis will indicate open spots, such as which of the 10 priority actions have not been well addressed yet and suggest ways to address them by 2015. An analysis of opportunities and threats to the successful implementation of the Action Plan at EU and national level will provide new information. Based on this analysis, recommendations for the second half-period of the Action Plan will be drafted. The final report shall include a list of Member State-specific recommendations on how respective Member States can improve their Action Plan implementation, as well as further recommendations concerning the work at EU level, for the Commission and the whole European group of Competent Authorities in the field.



### Published ACTOR study:

[http://ec.europa.eu/health/blood\\_tissues\\_organs/docs/organs\\_actor\\_study\\_2013\\_en.pdf](http://ec.europa.eu/health/blood_tissues_organs/docs/organs_actor_study_2013_en.pdf)

### Project consortium:

NIVEL, Netherlands institute for health services research  
Otterstraat 118-124  
3513 CR Utrecht  
NETHERLANDS  
Tel. +31 302729-700/647  
Fax +31 302729729  
E-mail: [r.friele@nivel.nl](mailto:r.friele@nivel.nl) Consortium

### Partners:

- Katholieke Universiteit Leuven (KULeuven), Leuven, Belgium
- Spanish Ministry of Health, Madrid, Spain

### EC contribution

This study has been funded by the European Union in the framework of the **Health Programme 2008-2013** (Service Contract: 20116141).

## Living Organ Donation in Europe (EULOD)

*This coordinated action has received co-funding from the European Union in the framework of the 7<sup>th</sup> Research Framework Programme.*

Organ scarcity is a serious problem in most EU Member States and results in long waiting times and high waiting list mortality in respect of all organs. Living donation is a valuable alternative to increase the amount of available organs for donation. Living organ donation means opportunities but also poses specific ethical, legal and psychosocial implications and challenges such as inequality in access to care, the risks for living donors and the growing problem of commercialism in organ transplantation and medical tourism.

European countries vary in terms of living organ donation practices, rates and ethical concerns, as well as legislation and protection systems for living donors. The Action Plan on Organ Donation and transplantation (2009–2015): Strengthened Cooperation between the Member States, put forward by the European Commission, emphasises the potentials of sharing experiences between Member states and promotes the exchange of best practices on living donation programmes (Priority Action 3).

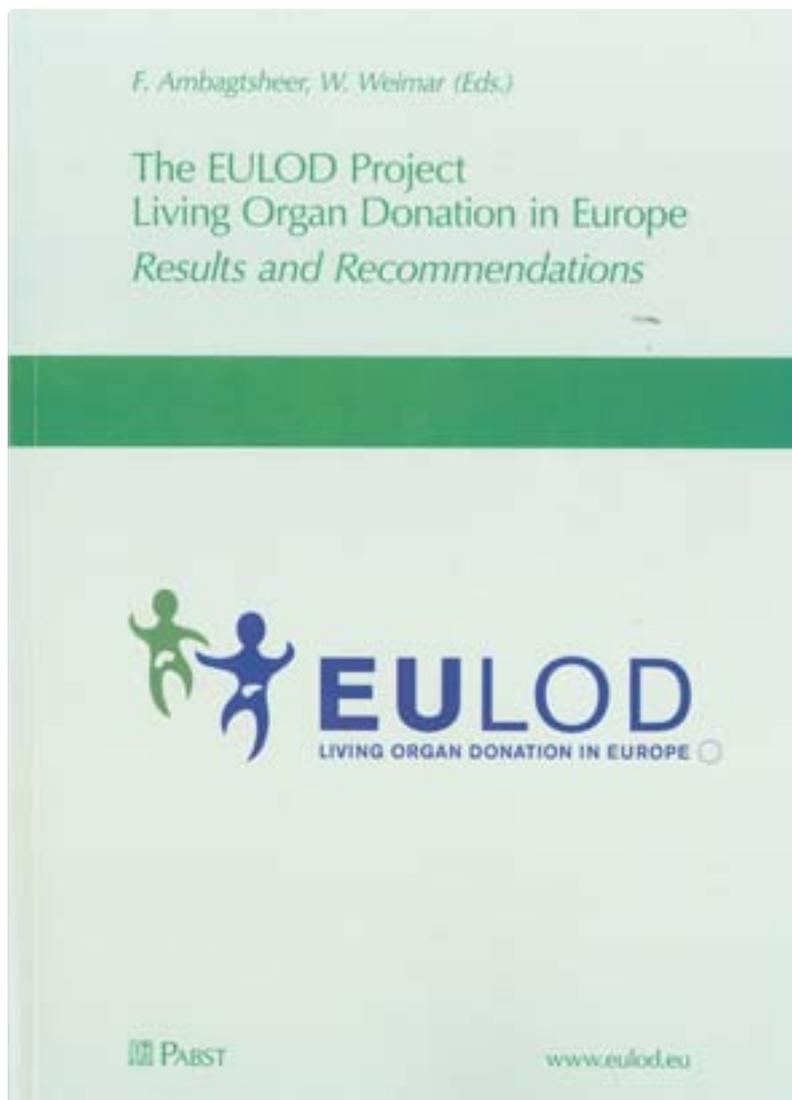
The objectives of the EULOD project are to establish an inventory of living donation practices in European Member States; to explore and promote living donation as a way to increase organ availability; and to develop tools that improve the quality and safety of living organ donation in Europe. The project aims to focus on the new EU Member States. Eleven partners from 10 different countries are involved in EULOD, where more than half of the participating organisations are from new EU Member States.

The project draws upon the support, knowledge and network of ELPAT — The European Platform on Ethical, Legal and Psychological Aspects of Organ Transplantation and ESOT — the European Society for Organ Transplantation.

The EULOD project started in April 2010 and finished in March 2012. It was managed by Erasmus University Medical Centre Rotterdam. To achieve these objectives, the activities were divided into two scientific research packages focusing on living unrelated donation practices and on the legal restriction and safeguards of living donation.

### Living unrelated organ donation practices in Europe

This work package collected data via an online survey on a wide range of aspects connected to living donation practices, such as prevalence and types of living organ donation; legal, ethical, financial and practical barriers. Data came from kidney and liver transplant centres in 40 European countries. Out of the then 27 EU countries, 25 were presented by kidney



*The EULOD Project Living Organ Donation in Europe — Results and Recommendations, by Ambagtsheer, F.; Weimar, W. (Eds.)*

transplant units and 18 countries by liver transplant units. The study resulted in a review of the various practices of organ donation in Europe. Almost all centres had a donor follow-up. National or European living donor registers were kept in 66 % of the kidney transplant centres and in 46 % of the liver transplant centres.

### Attitudes, barriers and opportunities: results from focus groups conducted in four European countries

Furthermore, the project performed a literature review to explore the ethical, legal, political, cultural, religious and profession-based arguments for and against living donation. Additionally, it conducted altogether four focus groups in Estonia, Bulgaria and Romania (all countries with low living donation rates), as well as in Belgium to better understand potential barriers towards living organ donation. The findings are being published in scientific publications.

### Legal restrictions and safeguards for living donation in Europe

A second major strand of the EULOD project focused on research about unrelated organ donation as well as organ trafficking and transplant tourism. With the help of ELPAT it identified and contacted legal experts on living organ donation in almost all European countries. These experts were asked to provide information on national living organ donation laws, anti-organ-trafficking laws, living donation practices and national legal systems. This information then was analysed, and results compiled in reports.

The report 'Comparative analysis of European transplant laws on living organ donation' provides an overview of these laws and reconsiders all legal requirements for living organ donation such as the concept and requirements of informed consent, classes of donors, restrictive measures, subsidiarity, procedural issues and social security regulations for donors. The report outlines that overall, almost all of the countries considered have established specific rules for Living Organ Donation, but only some regulations are comparable and great differences exist.

Furthermore, a final report is available on the EULOD website entitled 'Improving the Effectiveness of the Organ Trade Prohibition'. The report gives an overview of the role

“ We also want to investigate the obstacles that prevent the use of living donors, to highlight living donation as a way of increasing the availability of organs for transplants, and to produce guidelines that improve the quality and safety of living organ donation in Europe. ”

Annette Lennerling, Institute of Health and Care Sciences, Sahlgrenska Academy, Goteborg, Sweden <sup>(169)</sup>

of international organisations and their legal instruments against organ trafficking, transplant commercialism and transplant tourism. It furthermore describes the implementations of laws in these fields into national legislation in selected countries such as Hungary, Moldova, the Netherlands, Romania and Serbia. It also presents empirical data of field studies conducted in selected European countries, namely Moldova, the Netherlands, Romania and Kosovo, through stakeholder interviews, media analysis and archival research. Finally, the report provides a set of recommendations to improve organ trade prohibition in relation to different areas such as law enforcement, healthcare professionals, ethics committees and incentives.

### Better insights in the way European societies deal with the option of living unrelated donation

EULOD used various dissemination methods to reach its wide range of targeted stakeholders. Scientific articles were submitted for publication in peer-reviewed journals. EULOD has delivered numerous presentations about the project and its results have been presented at various national and international conferences.

Furthermore, the EULOD project is compiling the project reports into a book to be published and disseminated towards its main target groups such as competent authorities, transplant organisations and professionals, policy-makers and further relevant stakeholders in living donations.

As all participating project partners are ELPAT members, the project devoted special attention

<sup>(169)</sup> [http://www.sahlgrenska.gu.se/english/news\\_and\\_events/news/News\\_Detail/eu-funding-for-european-living-organ-donation.cid948345](http://www.sahlgrenska.gu.se/english/news_and_events/news/News_Detail/eu-funding-for-european-living-organ-donation.cid948345)

to integrate its work into the larger ELPAT (European Platform for Ethical, Legal and Psychosocial Aspects of Organ Transplantation) and ESOT (European Society for Organ Transplantation) networks. As part of this, two ELPAT working group meetings were organised in Sofia in October 2010 and in Berlin 2011 to discuss project plans and processes, evaluation and dissemination efforts.

Information on the project and its results have been published in four ELPAT newsletters to its contacts of around 9 000 people in the world. These newsletters can be found on the EULOD project website.

The final results of the project are expected to lead to a better understanding of the comprehensive aspects of living unrelated donation in Europe. EULOD therefore is expected to contribute generally to the improvement of the quality and safety for human organs, promotion of good medical practices and the identification of relevant research areas and future needs.

The project also responded to the need to communicate and exchange best practices on living organ donation programmes among EU Member States, and the need to enhance organisational models of organ donation and transplantation in order to relieve the current shortage.



### Further information:

Project website  
<http://www.eulod.eu>

DG Research and Innovation  
[http://ec.europa.eu/research/health/public-health/health-systems/projects/living-donation\\_en.html](http://ec.europa.eu/research/health/public-health/health-systems/projects/living-donation_en.html)

### Project team:

Kidney Transplant Unit, Internal Medicine,  
Erasmus Medical Centre  
Rotterdam  
NETHERLANDS  
E-mail: [j.ambagtsheer@erasmusmc.nl](mailto:j.ambagtsheer@erasmusmc.nl)  
Tel. +31 642668336  
Fax +31 104366372

### EU contribution

This coordinated action has received co-funding from the European Union in the framework of the **7<sup>th</sup> Research Framework Programme**.



**European Commission**

**Transplantation and Transfusion** — Projects and Actions for saving and improving the quality of life of citizens by facilitating transplantation and blood transfusion in the European Union

Luxembourg: Publications Office of the European Union

2013 — 195 pp. — 21 × 29.7 cm

ISBN 978-92-9200-020-2

doi:10.2818/14909





