



# **Workshop on Harmonising of Legislation in the Field of Transplantation of Human Organs**

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**Thursday 12<sup>th</sup> of December 2019  
Nemanjina 22-26, Belgrade, Conference room**

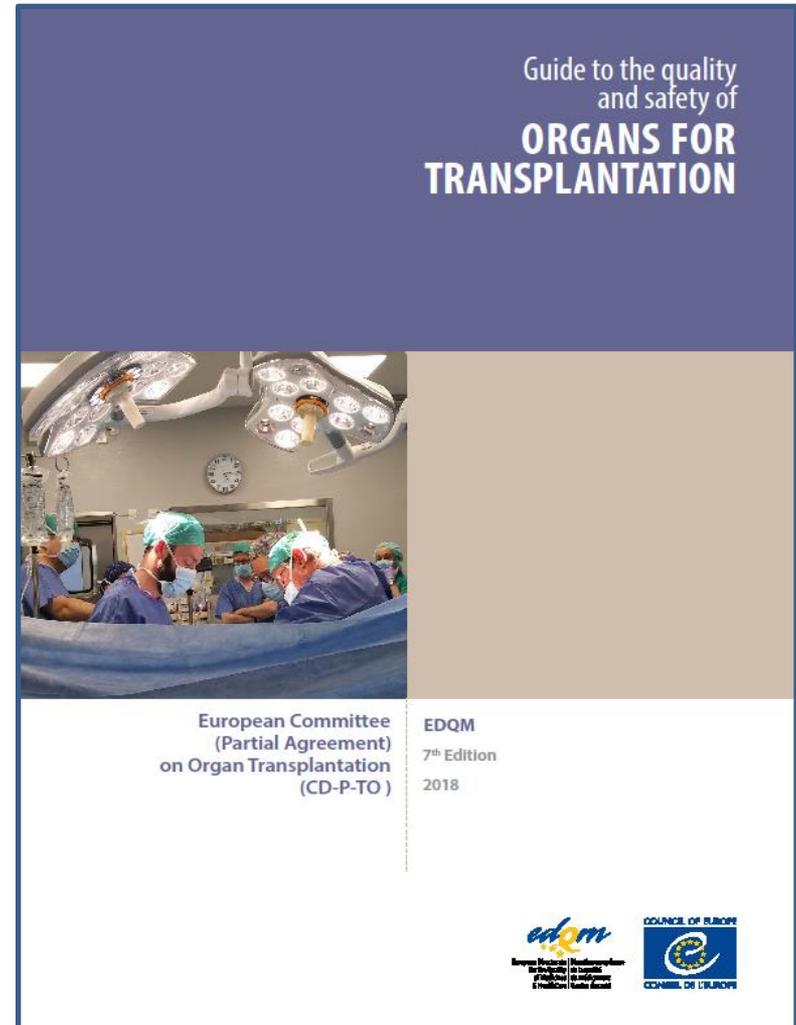


# Professionals standards

## EU AQUIS

**DIRECTIVE 2010/45/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**

**COMMISSION IMPLEMENTING DIRECTIVE 2012/25/EU of 9 October 2012 laying down information procedures for the exchange, between Member States, of human organs intended for transplantation**



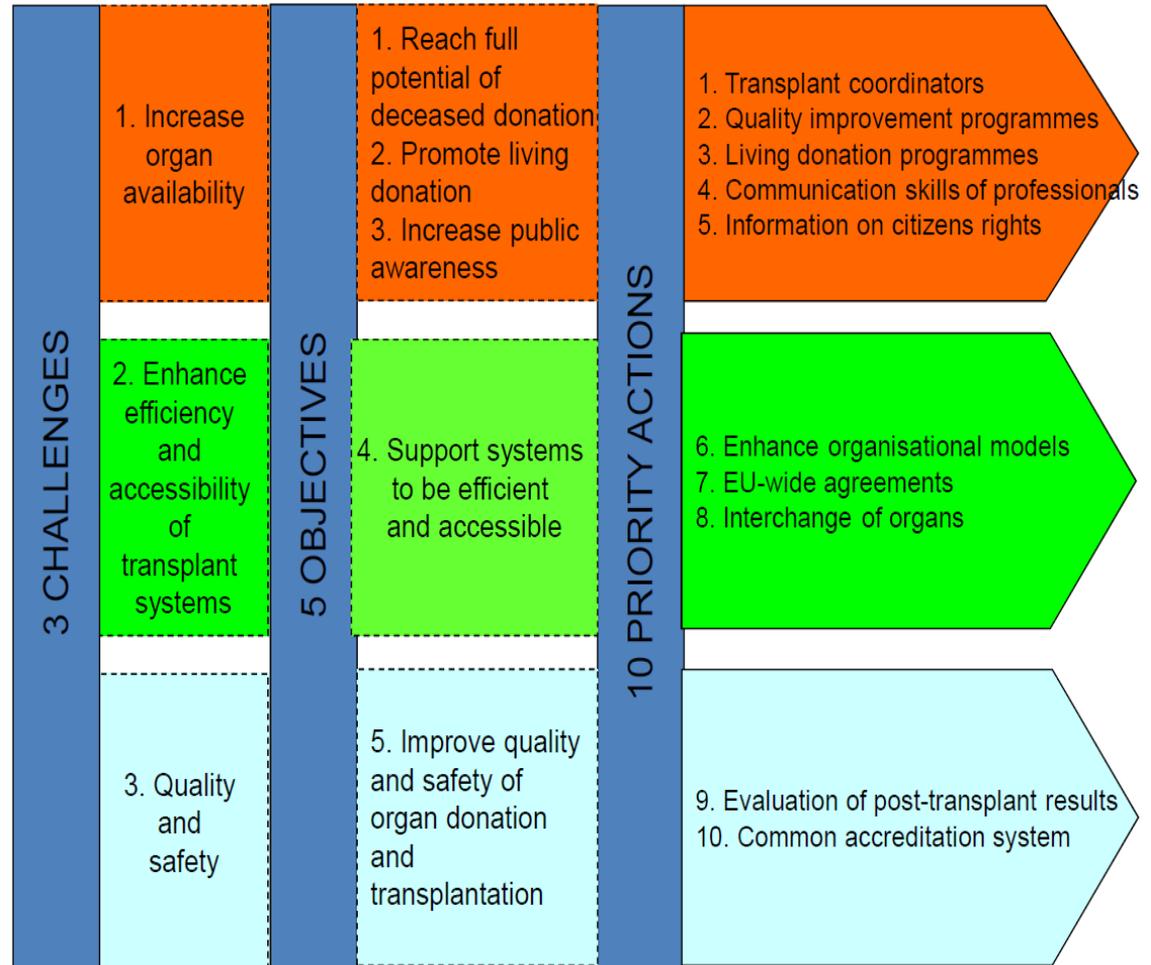


# Action Plan on Organ Donation and Transplantation (2009-2015): “Strengthened Cooperation between Member States”.

## INCREASE ORGAN AVAILABILITY

## ENHANCE EFFICIENCY AND ACCESSIBILITY OF TRANSPLANT SYSTEMS

## IMPROVE QUALITY AND SAFETY





## **The competent authority shall, in particular, take the following measure**

- a) establish and keep updated a framework for quality and safety
  
- b) ensure that procurement organisations and transplantations centres are controlled or audited on a regular basis to ascertain compliance with the requirements of this Directive;



# The competent authority shall, in particular, take the following measures

- (c) grant, suspend, or withdraw, as appropriate, **the authorisations of procurement organisations or transplantation centres** or prohibit procurement organisations or transplantation centres from carrying out their activities where control measures demonstrate that such organisations or centres are not complying with the requirements of this Directive;
- (d) put in place a **reporting system and management procedure for serious adverse events and reactions** as provided for in Article 11(1) and (2);
- (e) issue appropriate **guidance to healthcare establishments, professionals and other parties** involved in all stages of the chain from donation to transplantation or disposal, which may include guidance for the collection of relevant post-transplantation information to evaluate the quality and safety of the organs transplanted;
- (h) ensure that the fundamental right to **protection of personal data** is fully and effectively protected in all organ transplantation activities, in conformity with Union provisions on the protection of personal data, in particular Directive 95/46/EC.



# EU DIRECTIVES REQUIREMENTS

- **Training requirements and principles for the SoHO inspection**
- **Requirements for *Kidney paired donation program***
- **International exchange of organs and collaboration with Organ Exchange Organisation**



# Professionals standards

## Guide to the quality and safety of **ORGANS FOR TRANSPLANTATION**



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## Guide to the Quality and Safety of **TISSUES AND CELLS** for Human Application



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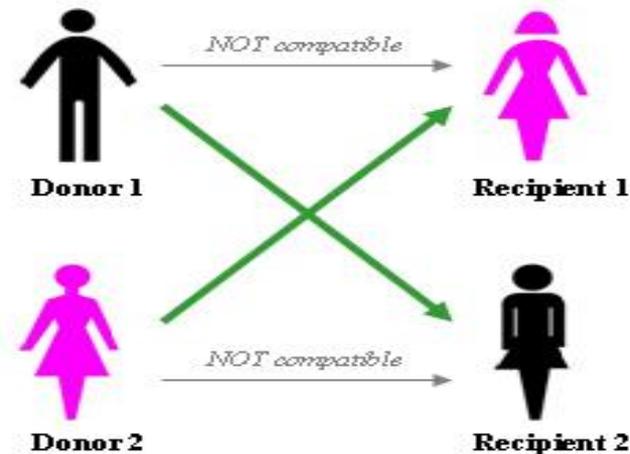
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# Paired exchange program

Sometimes a loved one may want to donate a kidney but their blood type is incompatible. Some transplant centers will help incompatible pairs of recipients/donors through a process called paired exchange, which involves two living donors and two recipients.

If the recipient from one pair is compatible with the donor from the other pair, and vice versa— the transplant center may arrange for a "swap"—for two simultaneous transplants to take place. This allows two transplant candidates to receive organs and two donors to give organs though the original recipient/donor pairs were unable to do so with each other.



**Figure 1:** In paired exchange, an incompatible donor/ recipient pair (such as a mother and son that don't have compatible blood types) are matched with another incompatible donor/recipient pair for a "swap". Each donor gives a kidney to the other person's intended recipient.

# Never Ending Altruistic Donor (NEAD) chain

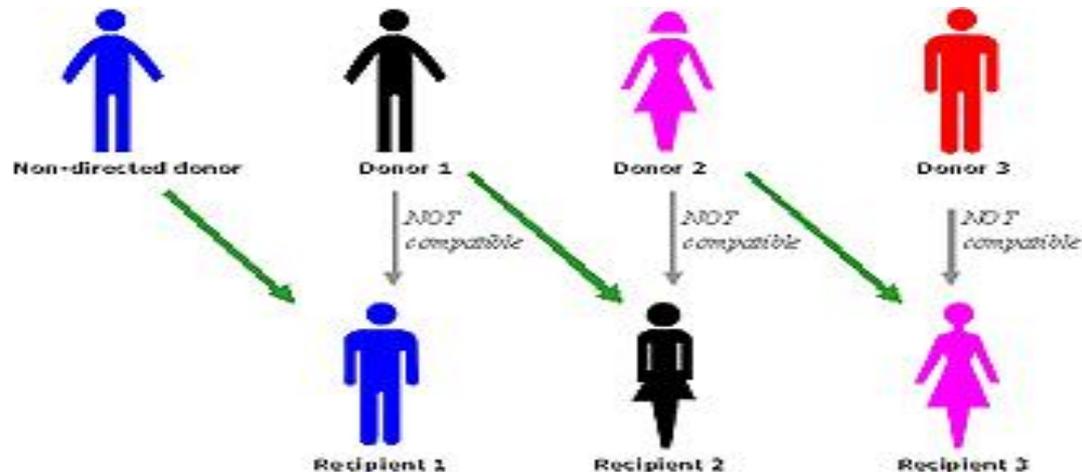
Never Ending Altruistic Donor (NEAD) chain

A NEAD™ chain (Never Ending Altruistic Donor chain) begins with one non-directed (altruistic) potential donor. In this program, the non-directed donor gives to a person waiting for a transplant, and that recipient's willing – but incompatible – donor gives to another person waiting, and so on.

Each living donor in this system gives to a stranger, and the chain of donors is kept going as long as possible.

**Figure 2:**

*In A NEAD™ chain, a non-directed donor gives to a recipient, and that recipient's willing – but incompatible – donor gives to another person waiting, and so on.*





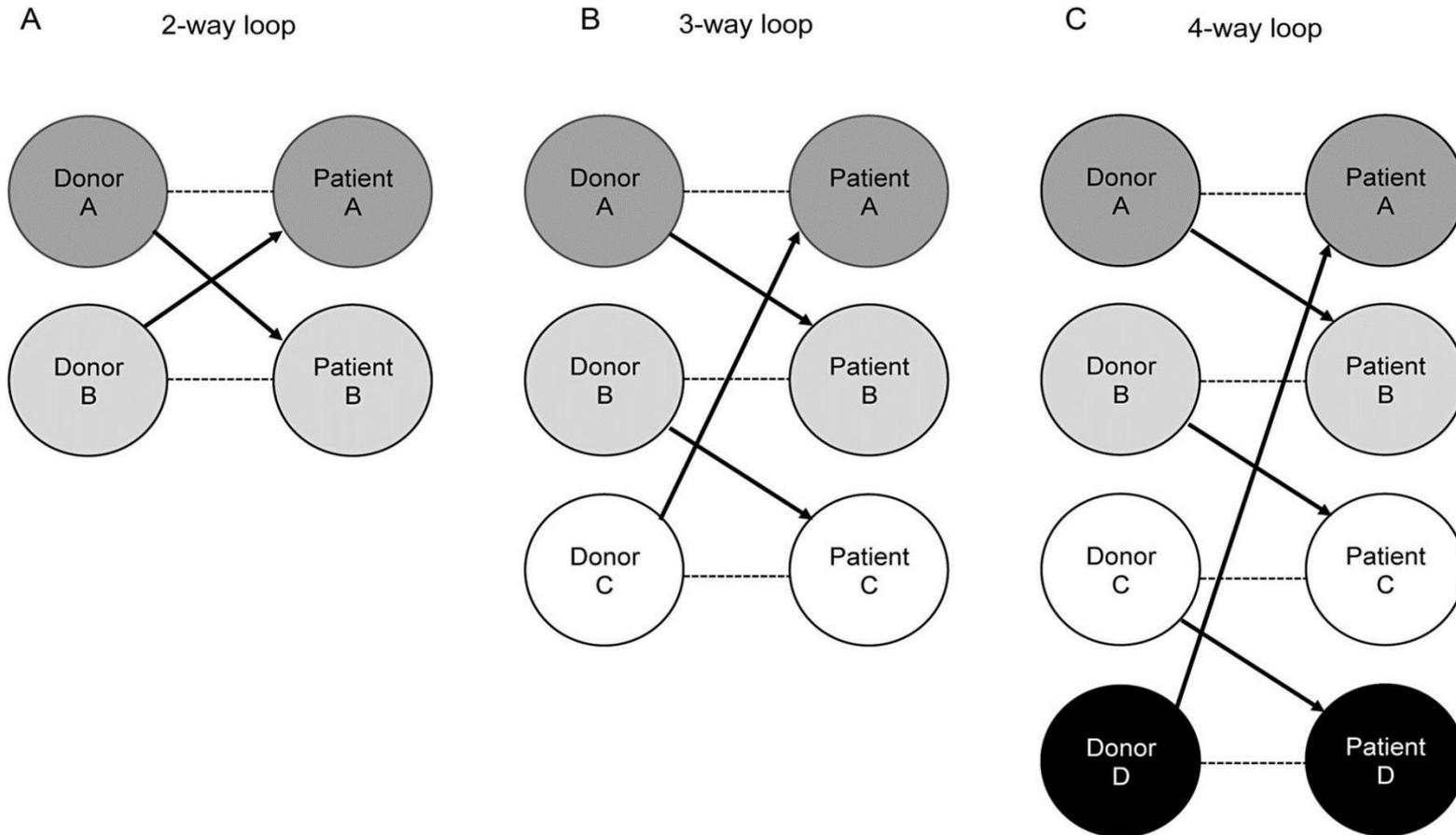
Incorporation of non-directed anonymous donors (NDAD), also known as Good Samaritan or altruistic donors, into a KPD registry, can initiate many more transplants without obligatory matching of a paired recipient, and guaranteeing a minimum of two transplants via 'domino' chains.

Such chains, initiated by an NDAD, are terminated with the last paired registered donor donating to a wait-list recipient or waiting as a bridge donor, to initiate a future NDAD chain.



**In ‘conventional’ KPD using these closed loops of two or more pairs, transplants must be simultaneously performed to guarantee all recipients receive a transplant and eliminating the risk of any donor withdrawing their consent leaving an orphaned recipient.**

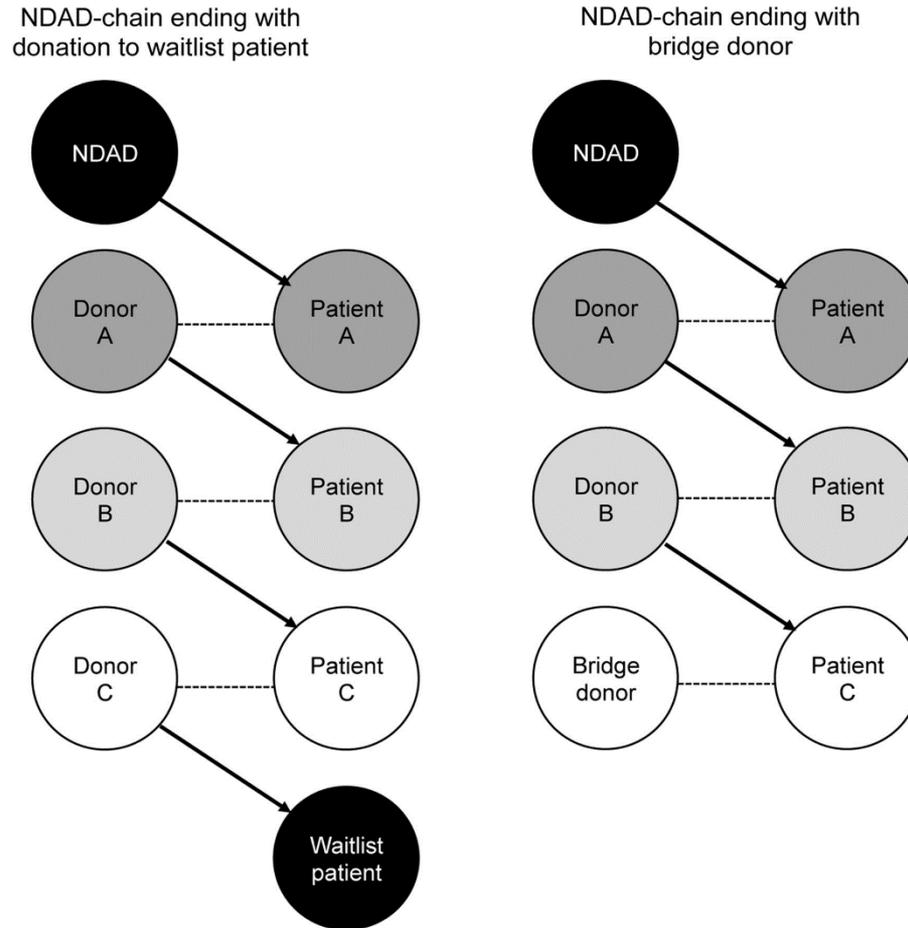
**FIGURE 1:** Exchange strategies in KPD. (A) A conventional two-way loop exchange between two incompatible donor–recipient ...

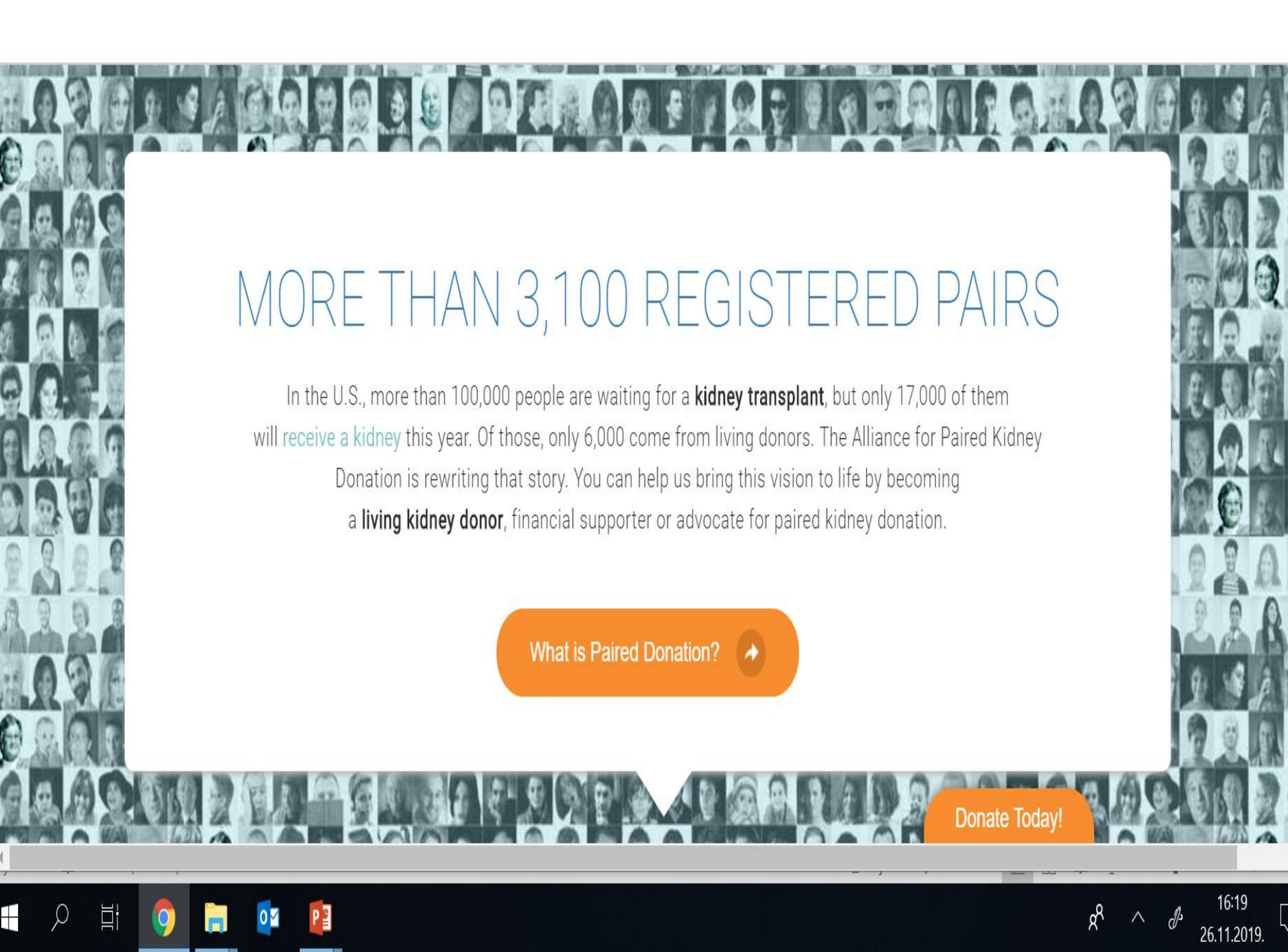




Conventional KPD transplants  
require incompatible pairs to be matched to  
other pairs with reciprocal incompatibilities,  
which may be challenging when only  
few pairs are available

**FIGURE 2:** Multiway exchanges beginning with an NDAD and including multiple donor–recipient pairs. (A) The closed chain ...





# MORE THAN 3,100 REGISTERED PAIRS

In the U.S., more than 100,000 people are waiting for a **kidney transplant**, but only 17,000 of them will **receive a kidney** this year. Of those, only 6,000 come from living donors. The Alliance for Paired Kidney Donation is rewriting that story. You can help us bring this vision to life by becoming a **living kidney donor**, financial supporter or advocate for paired kidney donation.

What is Paired Donation? 

Donate Today!





# Kidney paired donation

**Single centers**

**Multicenters**

**National registers**

- **Sophisticated algorithms to identify optimal match potential**



- Rapaport [10] first introduced the concept of KPD almost 30 years ago. **South Korea**, a nation with limited access to deceased donors where the majority of transplants are reliant on the live-donor source, was the first country to report the establishment of a KPD program in 1991.
- Following the Korean experience a number of single-center, regional and national KPD registries have been established.
- Single-center KPD transplants have been reported from several countries including Romania, Turkey and India.
- Multicenter, integrated, national registries have been reported to date from four countries: the Netherlands UK Canada and Australia



**Donors are usually typed at a minimum for HLA-A, -B, -C, -DR, -DQ and in some registries -DQA, -DPA, -DPB and -DRB3/4/5 typing is also included.**

**Acceptable mismatches are identified by excluding donors with HLA antigens to which a particular recipient has DSA.**

**The set threshold for acceptable DSA can vary from serological methods to highly sensitive single antigen beads technology.**



Almost invariably, all major KPD registries use a **virtual cross-match** approach to allocate suitable donors in the pool to registered transplant candidates, although the extent of HLA-antigens included in the virtual cross-match algorithm varies among registries



# Match scores (UK)

**A score is calculated for each potential transplant in an exchange, based on the following factors:**

**Previous matching run points<sup>3</sup>** – the number of quarterly matching runs in which the recipient has previously participated, multiplied by 50

**Sensitisation points** – 0-50 points (for 0-100% sensitised)

**HLA mismatch points** – 15, 10, 5 or 0 points for mismatch levels 1, 2, 3 or 4, respectively

**Donor-donor age difference points** – 3 points awarded if donor-donor age difference < 20 years

**Local exchange points<sup>5</sup>** – 20 points for local exchanges within 5 areas of the UK

**Table 1.**

Key ingredients of four national kidney paired donation registries

Country	The Netherlands	UK	Canada	Australia
Year established	2004	2007	2009	2010
Name of program	Living Donor Exchange Programme	National Living Donor Kidney Sharing Scheme (NLDKSS)	Canadian Blood Services Kidney Paired Donation Program (CBS-KPD)	Australian paired Kidney eXchange Program (AKX)
Dedicated central support staff	Yes	Yes	Yes	Yes
HLA laboratories involved	Single	Multiple	Multiple	Multiple
Types of exchanges considered	Multiway and domino	Multiway and domino	Multiway and domino	Multiway and domino
Accepts ABO-incompatible donor matching	No	Yes	No	Yes
Donor travel or organ transport	Donor travel	Organ transport	Donor travel (rarely organ transport)	Organ transport
Frequency of match cycles	Every 3 months	Every 3 months	Every 4 months	Every 3 months
Donor allocation algorithm	Virtual cross-match	Virtual cross-match	Virtual cross-match	Virtual cross-match
Primary allocation criteria	Unacceptable antigens based on recipient's serological DSA for HLA-A, B, Bw, DR, DQ	Negative virtual cross-match at HLA-A, B, C, DRB1, DRB345, DQB1, DPB1	Negative virtual cross-match at HLA-A, B, C, DRB1, DRB345, DQA1, DQB1, DPA1, DPB1	Negative virtual cross-match at HLA-A, B, C, DRB1, DRB345, DQA1, DQB1, DPA1, DPB1

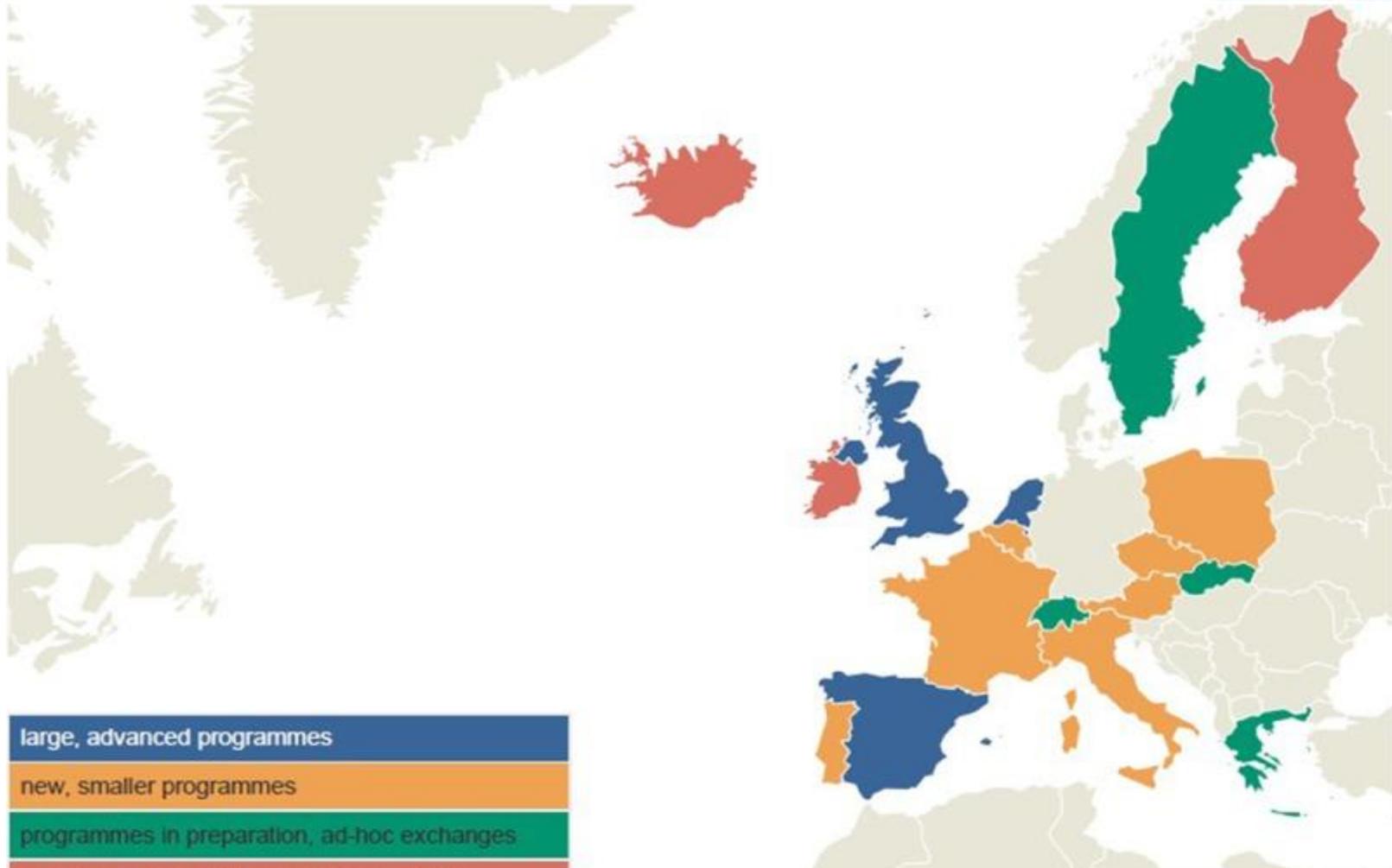


## KPD combined with ABO-incompatible transplantation

Given the excellent outcomes of ABO-incompatible transplantation in the absence of DSA an additional strategy to increase options for sensitized patients is to accept kidneys from ABO incompatible, but HLA acceptable donors within an existing KPD pool

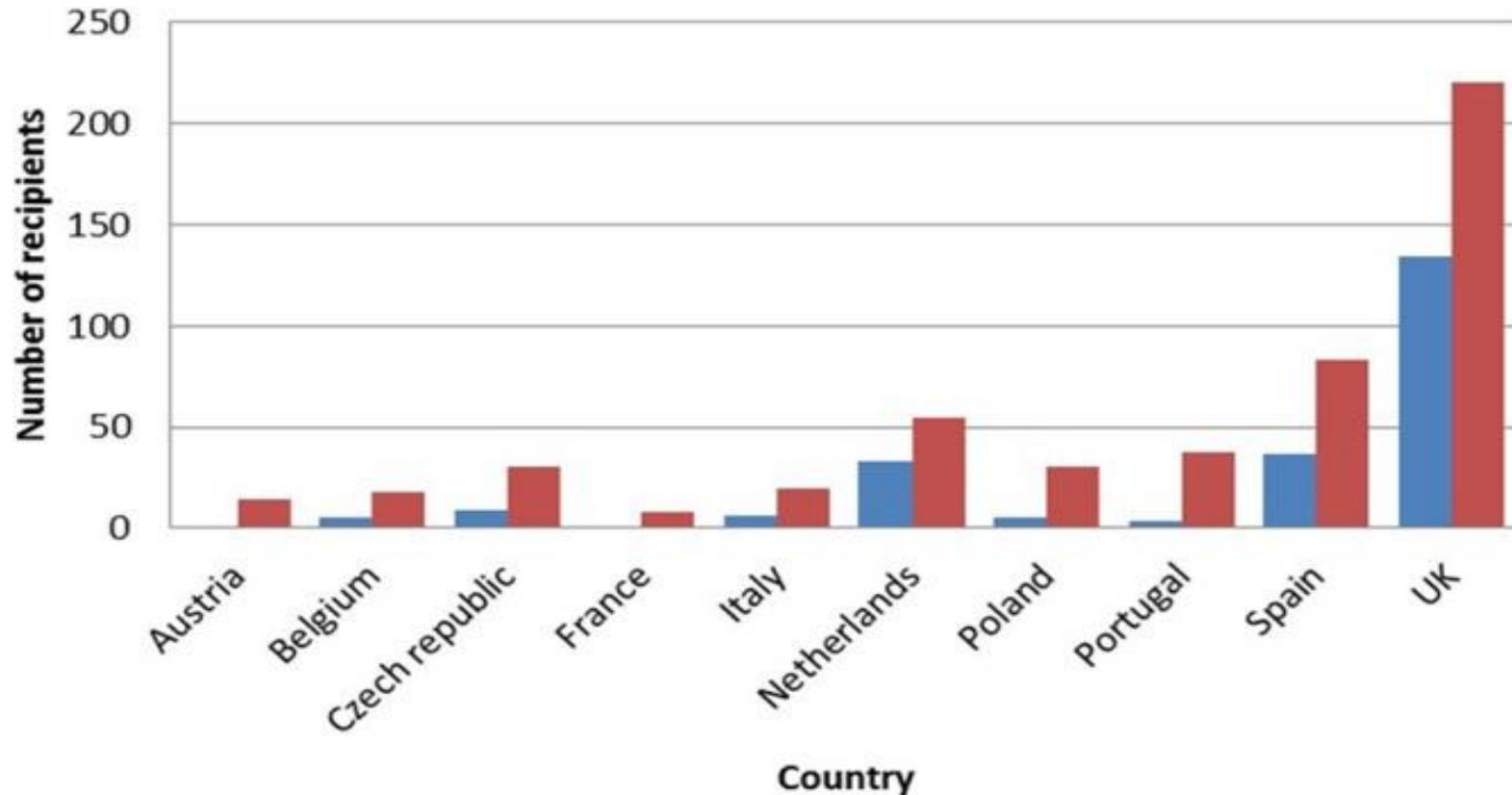
In the **Australian** program each participating center may register recipients **for ABO-incompatible matching** based on center expertise in managing ABO-incompatible transplantation and the recipient's baseline anti-blood group antibody titer.

The maximum baseline titer considered acceptable to attempt an ABO-incompatible transplant is generally below **1 : 64 by microcolumn agglutination technology**.



[Transplantation. 2019 Jul; 103\(7\): 1514–1522](#) Building Kidney Exchange Programmes in Europe—An Overview of Exchange Practice and Activities

## Number of recipients transplanted (blue) and newly registered (red) in KEP in 2015



[Transplantation. 2019 Jul; 103\(7\): 1514–1522](#) Building Kidney Exchange Programmes in Europe—An Overview of Exchange Practice and Activities



Paolo Ferrari, Willem Weimar, Rachel J. Johnson, Wai H. Lim, Kathryn J. Tinckam, Kidney paired donation: principles, protocols and programs, *Nephrology Dialysis Transplantation*, Volume 30, Issue 8, August 2015, Pages 1276–1285, <https://doi.org/10.1093/ndt/gfu309>



# **PREDMET INSPEKCIJSKOG NADZORA**

**sistem za kvalitet i bezbednost  
organa za presađivanje**

**zaštita dostojanstva, prava i  
zdravlja primaoca i davaoca**

**vođenje republičke liste  
čekanja i evidencija**

**sistem dodele i razmene  
organa**

**primena etičkih načela jednake  
dostupnosti i dobrovoljnosti**

**Pravilnik o bližim  
uslovima u pogledu  
stručne osposobljenosti,  
stručnog usavršavanja,  
kao i smernicama u vezi  
sa vršenjem  
inspekcijskog nadzora, na  
osnovu člana 46. stav 5.  
Zakona o presađivanju  
ljudskih organa ("Službeni  
glasnik RS", br. 57/18**



# **Direktiva Komisije 2012/25/EU o načinu izveštavanja o razmeni ljudskih organa namenjenih presađivanju između država članica.**

# **Pravilnik o načinu nacionalne saradnje, kao i saradnje sa međunarodnim telima ili evropskim organizacijama za razmenu organa**



# **Pravilnik o načinu nacionalne saradnje, kao i saradnje sa međunarodnim telima ili evropskim organizacijama za razmenu organa**

- 1. Razmena informacija o davaocu organa**
- 2. Razmena informacija za dodelu organa**
- 3. Razmena informacija o presađivanju organa**
- 4. Razmena informacija kod međunarodne razmene organa**



# Direktiva Komisije 2012/25/EU

## Područje primjene

Ova se Direktiva primjenjuje na prekograničnu razmjenu ljudskih organa namijenjenih presađivanju unutar Europske unije.

## Predmet

- (a) postupci za prijenos informacija o **karakterizaciji** organa i darivatelja;
- (b) postupci za prijenos informacija koje su potrebne, kako bi se zajamčila **sljedivost** organa;
- (c) postupci kojima se jamči izvješćivanje o ozbiljnim **štetnim događajima i reakcijama**



# Uprava za biomedicinu

- Dostavu informacija o karakteristikama donora i organa (**DONOR INFO**)
- Dostavu podataka o darovanom/primljenom organu; **JIB, datum, kontakt podatke centra**
- Razmjenu informacija o ozbiljnom štetnom događaju ili neželjenoj pojavi **SAR/E REPORT**



# HVALA NA PAŽNJI!