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Legal aspects of innovative transplantation technologies in ophthalmology in the light of the law in Bulgaria and other European countries

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The materials for the defense are available at the Scientific Department of MU-Varna and are published on the university's website.

CONTENTS

INTRODUCTION

For the purposes of transplantation, tissues and organs are needed, which must be donated by a living person or by a cadaveric donor after the consent of the relatives. This is a complex and intricate procedure that includes legal, social, religious and psychological aspects. In ophthalmology, transplantation requires the presence of corneal tissue and/or amniotic membrane. These are two types of donation, different in nature. Corneal tissue is taken postmortem according to all the rules for tissue donation and requires quick action. In Bulgaria, cornea donation encounters difficulties due to insensitivity on the part of the deceased's relatives, who are left with the feeling that the donor's "eyes are being taken" and his orbits remain empty. The Bulgarian proverb "went away with his eyes open" additionally creates emotional tension when making a decision to donate eye tissue at a national level. This requires researching and analyzing the desire for "cornea donation" on the part of relatives, paying special attention to the information that authorized persons receive before making a decision for donation on ocular tissue. At the same time, there is a growing need from donor corneal tissue. Therefore, it is appropriate to attempt to assess the processes and regulatory procedures related to corneal transplantation in the context of European trends and good practices.

Donation on amniotic membrane is different and accessible act on generosity. A donor can be a healthy mother who gives birth by cesarean section, as one membrane can numerous transplants and bioproducts are made. Amniotic membrane is a “biological waste” that cannot be of use to the mother or the baby, unlike the umbilical cord or placenta. This is also the reason why most mothers with planned cesarean births are willing to donate this tissue to a good cause. In Europe, amniotic membrane can be treated as a medical device, a biological product or a transplant (1-5). However, only the latter option is recorded in the registers, which makes the whole system extremely difficult to track. Amniotic membrane is used in various forms – in drops, powder and other varieties, which in turn

makes it difficult to assess both the role of transplantation for ophthalmology and the amount of donated and transplanted tissue.

In the Republic of Bulgaria, this problem is even more complicated, as there is no law on biological products. This legislative emptiness is serious regulatory obstacle in the practice. The analysis of the effect of the lack of legal regulations in this area will contribute to improving the activities of tissue banks and transplantation in Bulgaria and is of particular importance for improving the entire process of combating impaired vision and blindness.

Organ transplantation, fabrics and cells is huge achievement in medicine. This dissertation labor follows the historical emergence on the transplant surgery, particularly in ophthalmology. It examines some of its economic manifestations and contains a legal overview on legislative regulation in Republic Bulgaria and others countries from EU. The study attempted to derive good European practices that have helped to increase donor activity in other countries. The legal obstacles and economic obstacles to organ and tissue donation and transplantation in the Republic of Bulgaria have also been analyzed. Taking into account all these national and European features, this work was aimed at a systematic analysis of legislative norms and their interpretation in the context of tissue banking and transplantation in ophthalmology.

The study also indicates prospects for the development of new biological products and medical devices. The legal obstacles and economic difficulties in their application are outlined. The dissertation work pays special attention to the lack of awareness among the public about the need for organ and tissue donation; the lack of specially trained coordinators in medical institutions through which donation can be promoted; the absence of national campaigns through which accessible information can be disseminated to the population, allowing for a better understanding of the meaning and public benefit. from the noblest human act. In move on this research is developed and a proposed algorithm for optimizing donation, in connection with the work of donation coordinators at medical institutions, through which various mediation techniques can be applied and communication can be improved between the persons

appointed to this position and potential donors and their relatives and loved ones, authorized to make a decision on organ and tissue donation in donor situations.

I hope that this work will be useful, and I would like to thank my scientific supervisors for their valuable advice, the Department of Social Medicine and the Department of Eye Diseases and Vision Sciences for their methodological support. To my family, who have dedicated their lives to eye diseases and lead a daily struggle for more effective and rational protection of eye health, and most of all to my three-year-old son for his tolerance for me spending a long time at the keyboard instead of doing puzzles and Lego with him.

GOALS And TASKS

Purpose

To review, analyze and compare the legal framework and rules for organ and tissue donation and eye tissue transplantation in Bulgaria, in the context of European legislation and practice, and to build a hypothesis about the legality and application of innovative technologies and the practical implementation of bioproducts in the Republic of Bulgaria.

Tasks

1. A review of the published literature and an analytical reading of the legal provisions relating to tissue transplantation in ophthalmology.
2. Comparison of legal frameworks and clinical regulations for the application of tissues in ophthalmology in some European countries.
3. Identification of medical institutions - with the status of "tissue bank" and users of eye tissues in Bulgaria, according to the registration of the Medical Supervision Agency and quantitative analysis of activities related to eye transplantation in Bulgaria in authorized medical institutions, based on a survey among specialists engaged in these activities.
4. Collection, summary and analysis of information from public registers on eye tissue transplants performed in Bulgaria and leading European countries for the last 10 years.
5. Research into legal barriers and the reasons for low donor activity regarding eye tissues and formulating an algorithm for work that facilitates awareness of the population about the need for donation.
6. A look into the future – legal and ethical aspects of donation and transplantation in Bulgaria.

MATERIALS And METHODS

The study was conducted in the period 2021 - 2024 and is based on legislative framework, registers of published data on transplantation and exchange of organs and tissues in Bulgaria and Europe, and information obtained from our own questionnaire surveys. The medical aspects are based on public information and internal regulations of the Eye Bank Department of USBOBAL-Varna EOOD.

1. Analysis on legal regulation

In the process of implementing the tasks thus set to conduct a review and analysis of the legal, clinical, economic aspects and legislative provisions related to transplantation, and in particular transplantation in ophthalmology, the following theoretical methods were used:

- documentary method – applied to study the theoretical basis for national and European legislation;
- historical method – this method tracks the historical development of the researched objects;
- comparative method – this method compares the statistical results of studies, reports and registers in the Republic of Bulgaria and other European countries;
- legal method – used to compare national and European legislation in the research area;
- logical method – includes analysis, synthesis, comparison, summary of the studied phenomena and facts;
- graphical method – this method visually presents results;
- statistical method – used when processing data from analyses.

Detailed are national laws studied in Republic Bulgaria and the supranational EU regulations that relate to donation and transplantation.

2. Comparison on legal regulations and clinical regulations for application on tissues in ophthalmology in some European

countries

For analysis on legal regulation in row European countries are used public EU registers and regulatory documents published in English or French were studied. The following methods were applied: historical, comparative law, formalological and normative.

For the purpose of the study, 4 countries from the European Union were analyzed, namely: Italy, France, Spain and the Netherlands. The first three countries – Italy, France and Spain, were chosen due to the fact that they are leaders in the number of transplants performed per capita. The Netherlands was chosen due to the fact that it is the country in Europe with the most translational projects.

3. Identification on the medical restaurants – with status on "woven" bank and users of eye tissues, according to the registration of the Medical Supervision Agency and quantitative analysis on the activities related with ocular transplant in authorized medical institutions, based on a survey among specialists engaged in these activities

The register of medical institutions performing organ, tissue and cell transplantation activities is maintained by the Institute of Medical and Dental Medicine. Based on the issued permits, a geographical map of medical institutions performing transplantation activities in ophthalmology was made. The centers were divided into three groups:

-medical institutions carrying out activities related to the collection, processing, processing and distribution of tissues;

-medical institutions carrying out only transplantation activities;

-medical institutions carrying out all activities under the transplantation law.

The identified medical facilities were also classified based on the type of medical facility, expiration date of the permit, and specific transplantation activities in ophthalmology.

Registration for performing certain activities related to transplantation in Bulgaria does not have quantitative criteria. This determines the pronounced unevenness on a national scale. In order

to precisely determine the types of activities, their quantitative dimension and distribution across the country, a survey was created with two parts - one aimed at the medical institution, the other - at the specific specialists performing the activity. Based on the above considerations, a questionnaire was prepared and distributed to practicing doctors and other specialists working in the medical institution. The questions to the head of the medical institution are aimed at the importance of transplantation activities for the functioning of the medical institution. (Appendix 1)

The survey was distributed to all registered medical institutions, with group 1 (tissue banks) receiving only parts 1 and 3, group 2 (medical institutions with a transplant license in ophthalmology) - parts 1 and 3, and medical institutions performing all activities - the entire questionnaire.

4. Collection, summary and analysis on the information from public registers for the eye tissue transplants performed in Bulgaria and in leading is European countries for the last 10 years

To implement the first (national) part of this task, the register of the Executive Agency for Medical Supervision was used. A special table in Excel format was created, which collected information on the types and number of transplants performed in medical institutions for hospital and outpatient care. The results were analyzed in the context of the survey from task 4, in order to compare the data based on objective information and the subjective assessment of the performers of this medical activity. A snapshot from the IAMN website is presented in Fig. 7.

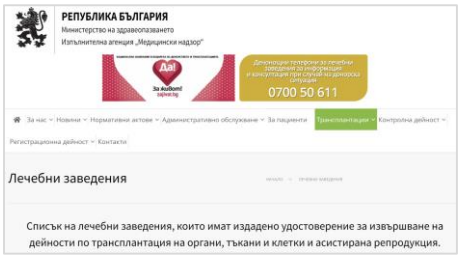

Fig. 1. Snapshot from the page on IAMN , demonstrating the organization on publicly available information

The EUROCET registry was used to carry out the second part of this task. The European Organ and Tissue Registry – EUROCET, is funded by a programme of the European Commission. The aim of the registry is to create, collect and update data from Member States in the field of organ, tissue and cell donation and transplantation activities. The registry helps to harmonise the terminology related to the transplantation process and the effective implementation of the European Directive EC 2004/23 setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells. The predecessor of EUROCET – EURODONOR, is another project funded by the European Commission, but operating from January 2003 to June 2004. EURODONOR covers only organ transplantation activities and does not include Eastern European countries. EURODONOR creates a good basis by building a network of countries willing to share their data and experience in the field of transplantation and donation. With the accession of ten new countries to the European Union, including those from Eastern Europe, it became necessary to create a register that would include both the old and new Member States of the European Union, and it was imperative to expand the scope of activities and the information maintained by the register. EUROCET started operating on 01.09.2005 as a useful source of information for the ministries of health in the different Member States, the European Commission, international organ exchange organisations, transplant centres, medical associations and societies, European and national health institutions, medical professionals, hospitals, patients and the general public by raising awareness and the importance of donation. At present, the EUROCET register aims to join all Member States of the European Union and aims to collect and maintain up-to-date information on national data on donation and transplantation and to compile a list of licensed tissue banks throughout Europe, in response to the requirements of Art. 10, p. 2 of Directive 2004/23/EC of the European Parliament and of the Council of 31.03.2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation , storage and

distribution of human tissues and cells.

Users of the EUROCET register have access to a large part of the data in the portal without having to register or provide identification information about themselves. The creation and maintenance of a register that has up-to-date information, such as EUROCET, is essential for the development and expansion of donation in European countries. On the one hand, the register implements the necessary harmonization of terminology in legal provisions and the interpretation of legal norms, as well as the creation of a common vocabulary necessary for the proper and rapid functioning of national systems in the field of donation and transplantation, as well as the international exchange of organs and tissues. On the other hand, the dissemination of reliable and up-to-date information is an essential element of this process, both for the general public due to the need for people to be informed about the need for charity in donation, and for improving the activities of institutions, transplant centers, medical specialists and all those involved in the donation and transplantation processes.

In the process on work with the register were reported the following imperfections:

- dynamics on the form in the years;
- voluntarily provision on the information from the countries member states;
- lack on regulatory regulation, which yes it affirm.

A special table in Excel format was created, which collected information on the types and numbers of transplants performed in European countries, registered for the specified period. A snapshot from the EUROCET website is presented as Fig. 2.

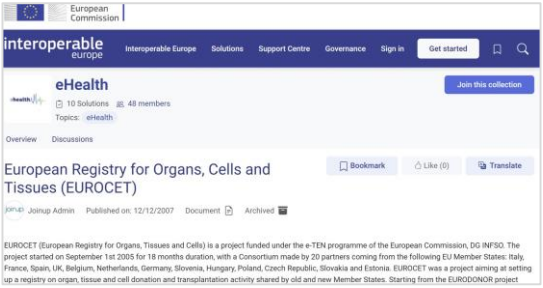

Fig. 2. Snapshot from the page of EUROCET, demonstrative the organization of publicly available information

5. Research into legal barriers and causes for the low donor activity and formulation on a work algorithm facilitating the population's awareness of the need for donation

The study analyzed the legal barriers to the export and import of tissues in the field of ophthalmology, using the EUROCET registry for this purpose, and examined the legal requirements and clinical pathways that thwart the possibility of the Republic of Bulgaria being both an importer and exporter of corneal tissue from and to third countries.

To improve the awareness of the population about the need for donation, some of the techniques used in mediation have been studied. Their application by specially trained coordinators in medical institutions, who possess verbal and communication skills, towards potential donors and their relatives would help to raise people's awareness and significantly increase donor activity on a national level. In this regard, an algorithm has been developed to improve the effectiveness of "donation coordinators", in cooperation with medical specialists in potential donor situations.

6. Look in the future – legal and ethical aspects on donation and transplantation in Bulgaria

Donation is the most noble act when it comes to organs and tissues. Human tissue is priceless and unfortunately in constant shortage. This circumstance requires the implementation of a set of measures by the countries to reduce the deficit. A synthesized review of good and useful practices in the national systems in various

European countries in the field of donation and transplantation has been made and a comparison with the shortcomings of the national legislative system and practical situation in the Republic of Bulgaria has been made. In addition, to improve the awareness of the population, an "information brochure" has been developed and printed, which is provided free of charge as an electronic file to all eye tissue banks in Bulgaria.

CHAPTER THREE. RESULTS

1. Overview on the published literature and analytical reading on legal regulations relating to tissue transplantation in ophthalmology

Each country applies different rules, regulations and provisions that regulate the donation of organs, tissues and cells. In some countries, it is adopted to maintain a national register or to have a donor card, in which each person must enter his/her consent or refusal to have his/her organs and tissues used for donation after his/her death. In other countries, the so-called "explicit refusal" is applied, according to which it is presumed in the legal world that if the person has not explicitly expressed his/her refusal during his/her lifetime, his/her organs and tissues can automatically be used in donation situations. However, in most European countries, in the absence of an explicit and duly expressed written refusal, the aforementioned registers and donor cards are only informative in nature. In such cases, in practice, the final decision belongs to the relatives and friends of the deceased person. Donation of organs and tissues from a living or cadaveric donor is only possible after all ethical and regulatory requirements according to European and national legislation have been met. From a legal perspective, the identity of donors and their relatives is protected information, and recipients are not able to establish direct contact with donors and their relatives. In some countries, the only option is for recipients to send a thank-you letter to the donor or his relatives.

Medical intervention in living donation may only be carried out after the donor has given his free and informed consent, after having received prior relevant information about the purpose and nature of the intervention, as well as about its consequences and risks, and taking into account the fact that the donor may freely withdraw his consent at any time.

All donation and transplantation activities, except those that are legally required, should be documented in writing. For this purpose, hospitals that perform activities related to establishing brain death, maintaining the vital functions of potential donors, explantation and

transplantation, and all other actions related to donor situations, are provided with special blank documents, in which all the details and details related to the above are recorded in detail. These documents include, but are not limited to: declaration of consent from the donor/his relatives, notifications and reports of serious adverse reactions and incidents, declaration of post-mortem care, notification of refusal of transplantation, and others.

Medical devices, on the other hand, have a special law that regulates the matter at the national level, namely: the Medical Devices Act, as well as a rich supranational framework of regulations and directives. The application of medical devices is hampered by economic factors - the high cost of acquiring a CE marking, as well as the highly restrictive registration system, the onerous procedure for placing them on the market or in operation. However, their application is possible and regulated in detail by law. On the other hand, in the legal world, the application of bioproducts is not regulated by law and their application is hindered. Although the transplantation of organs, tissues and cells in medicine is still indispensable with its life-saving functions, and in the field of ophthalmology it is the only alternative for improving and restoring the vision of people with permanent disability and blindness caused by corneal damage, the application of bioproducts undoubtedly has an extremely beneficial therapeutic effect, and with the advancement of medicine and new technologies, it is undoubtedly a useful and indispensable application. However, the national legislation of the Republic of Bulgaria lacks both an explicit law regulating the matter and sufficient provisions to support the application and distribution of bioproducts from a legal point of view. This legislative gap hinders the application of developed bioproducts and deprives many needy patients of their therapeutic effect. The reason for this is the lack of legal matter regulating their actual application. Biological products do not have an algorithm for forming the price, and in addition, it is not legally defined as the object of what type of transaction they should be treated as - refundable or free of charge. At present, they are only subject to a notification regime to the Executive Agency for Medical Supervision. In some

countries, processed tissues that, according to the national legal definition, meet the legal definition of "bioproducts", are registered as medical devices. In this case, their price could be freely determined on the market. An example of this is the medical device registered in the UK under the name "Omnigen", which essentially represents a lyophilized amniotic membrane. The price of this product is between 200 and 500 British pounds, and in Italy a medical device called "Chloroclar" has been registered, which in its essence corresponds to the legal definition of a "bioproduct", namely: the patient's own cells propagated on decellularized amniotic membrane. The price of this product is over 10,000 euros. The two above-mentioned products, which in their essence correspond to the definition of a "bioproduct" given in our national legislation, are registered as medical devices abroad. In connection with the above, the question arises, if in the Republic of Bulgaria such products are registered as medical devices, due to the lack of legal regulation for "bioproducts", and the price of these products is determined freely on the market, how will such expensive products be reimbursed. The lack of legislation in the field of bioproducts allows the use of market mechanisms that benefit private structures and medical institutions, but to the detriment of patients in need of treatment and therapy, who, according to economic parameters, are the consumers of the aforementioned products, for whom it would be extremely difficult to afford their application. At present, it is possible to register a custom-made medical device, representing a decellularized amniotic membrane with the recipient's own stem cells, which product would in its essence meet the legal definition of a bioproduct, but its application as a biological product is impossible and is thwarted due to the lack of detailed legal regulation for its financing, reimbursement and exploitation.

2. Comparison of legal frameworks and clinical regulations for tissue applications in ophthalmology in some European countries based on an online survey

Transplantation activities in Europe are registered in the unified EUROCET system. Thanks to a grant from the European Commission

and the efforts of the National Transplantation Centre in Italy, all national regulatory organisations have submitted their registered “suppliers” and “users” of organs, tissues and cells for transplantation, including tissues for transplantation in ophthalmology.

The study analyzes the main legal framework relating to donation and transplantation in several European countries that report the highest share of transplants performed per capita and the highest contribution to the field of donation.

FRANCE

Keratoplasty is most often the performed transplantation on fabrics in France (21, 97-99). Each year in the country is carry out around 5000 transplants on cornea. Through 1948 is created The Association in French ocular banks. One year later, through 1949 year, In France, a law was passed **on July 7, 1949** , known as the Lafayette Law, which legalized corneal explantation and transplantation, and according to which law the eyes on the deceased, which during life them is bequeathed on public or private medical institution, can be removed immediately after death. This law was repealed in 1994 and replaced by the first bioethics laws, and the fourth version of **the Bioethics Law** is currently in force .

It is noteworthy that the French Bioethics Law also defines the persons from whom patients in need can receive organs for transplantation during their lifetime. The law lists them exhaustively according to their family relationship with the recipient, namely: mother, father, son, daughter, brother or sister. Moreover, it is stated is, that at urgent cases donor can yes be and the husband on the recipient. Intended is and form for the prior informed consent from the donor, as consent should be declared before the court. It can be concluded from the legal provisions that only adults could be living donors in France, regardless of the declared consent of both the donor and his parents or guardians. An exception is made only for bone marrow donation, but even in this procedure there are certain restrictions (100).

In France, as in Bulgaria, the so-called "presumed consent" is

applied, according to which all citizens is consider for donors on organs, fabrics and cells, except if explicitly no are have expressed their unwillingness to do so. And in France national operates a register of refusals, in which every person has the opportunity to express his/her will not to be a donor after his/her death. Another statutory option provided for the person who does not wish to be a donor after his/her death is to draw up a written document in which to objectifies his will, as a mandatory condition is that the document be duly signed and dated by its author, and in case there is an objective impossibility for the document to be signed personally, it is necessary for two witnesses to certify with their signatures the will of the author of the document. In addition, the current principle of presumed consent requires the doctor to collect testimony from the deceased's family in connection with the decision to donate organs. The expressed consent or refusal is stored in the deceased's medical file. Among the innovations in the Bioethics Act, made in 2011, cross-donation in case of incompatibility between relatives was also legalized (101).

The possibility of using organs, tissues and cells from a deceased person is also enshrined in the provisions of the **French Civil Code** , where in Art. 16-3 it is provided that one of the exceptions to violating the integrity of the human body is the need for therapeutic needs of patients in need of transplantation. In Art. 16-8 of the same normative act is indicated and the explicit ban for disclosure on identity on recipient or donor. The following provisions of the French Civil Code also contain legal norms that prohibit both advertising for the availability of products for transplantation and conducting transactions or intermediary activities for the purpose of material gain from the explantation and transplantation of organs, tissues and cells.

In **the French Public Health Code** , and more specifically in the second part, in chapter three, the legislator has specified the procedure for removing organs, tissues and cells from a deceased person. In explantation, established practices are applied, drawn up by the Minister of Health, based on proposals from the Biomedical Agency.

Explantation, transplantation of organs and tissues and all accompanying processes of donation in France is coordinate from The Agency by biomedicine. The Agency acts under the control of the Ministry of Health. It was established by the Bioethics Act in 2004. The agency's competencies consist of activities for the coordination and distribution of organs and tissues, in accordance with medical criteria and principles of fairness, management of the national registry of patients in need of transplantation, as well as the national registry of persons who have declared their refusal to be postmortem donors during their lifetime, popularization of information on organ, tissue and cell transplantation and the need for donation. In addition, the Biomedicine Agency organizes trainings for health professionals in order to optimize the processes of detection and encouragement on potential donors and their families, as founded all own actions, citing respect for ethical principles in the law.

Eye banks in France are accredited by the French Agency for Health Safety of Health Products as a competent authority, according to criteria set by the Association of French Eye Banks and the French Society of Transplantation. Tissue banks in Brest and Saint-Etienne deliver more from half material for transplants on fabrics in France. Banks are part from The National French bloody institute, which has with a plurality tissue banks both in mainland France and in its overseas territories. Six of the institute's banks process and provide amniotic membrane. The Lille tissue bank is a functional unit of the Lille University Hospital. It supplies material for transplants in the field of ophthalmology, mainly in the northern part of Paris. The tissue bank, which operates under the Hospices civils de Lyon (HCL) foundation, is one of the few structures accredited by the French National Agency for the Safety of Medicines for the production of advanced therapy medicinal products (ATMPs), which are medicines for humane use, which are "based" on genes, cells or tissue engineering". Receiving on this one accreditation requires tissue bank yes answers on strict organizational criteria, technical skills of the staff, quality system, etc. The bank has internationally recognized experience in the field of production and preservation of cells and

tissues for therapeutic use, including the use of amniotic membrane as a substrate for cultivation and reproduction on cells. The fabric bank in Nancy is accredited by the National Agency for the Safety of Medicines in France for the collection, processing, processing, storage and distribution of tissues intended for transplantation, including corneas and amniotic membrane. The French Eye Bank is located in Paris. It has provided for the possibility of issuing a cornea donor card, which any person can apply for electronically during his lifetime (Fig. 3). It has no legal value, but only an informative nature about the wishes of the person who filled it out and to facilitate the cornea donation procedure in the event of death. The name of the bank implies that its activities are limited only to eye banking. In the city of Rouen, France, there is a Cornea Bank, which has specialized its activities in the processing and preparation of corneal material for transplantation. The bank receives donor material from 14 medical institutions and ensures its distribution for transplantation throughout France. Amniotic membrane is also processed in the corneal bank laboratory. Saint-Priest-en-Jarre is home to French laboratories, institutes and specialized centers equipped with specialized analysis equipment. on biological samples, fabrics and cells and others samples. The researchers in The laboratory also explores the possibilities for the development of medicine in the field of cell biology. They conduct is and trainings, in including practically. In one from the laboratories with Under the name "Biology, Engineering and Inventions for Ophthalmology", research is being carried out on the possibility of using tissue engineering in the field of transplantation in ophthalmology, biomedicine, and tissue banking.

Fig. 3. Donor map for donation on cornea, provided from French eye bank

ITALY

Every adult citizen of Italy has the opportunity during his lifetime to declare his preference. regarding donation on organs and fabrics after death you are. The foundation for this is regulated in **The law for transplants** n. 91/99, where in detail is established and the entire procedure for collecting, processing, processing, storing and distributing material for transplantation. In the absence of a will from the deceased, his family and relatives can declare in writing their consent to donate his organs and/or tissues postmortem. In Italy, an age restriction has been introduced in relation to corneal donors - their age must be between 4 and 79 years (25, 100, 102-105).

Eye banks in Italy are evenly located according to the regions in Italy. Accreditation and the inspection is performs from The National center for transplants as competent organ according to the Guidelines for the extraction, processing and distribution of tissues for transplantation purposes, prepared jointly by the Permanent Technical Council for Transplantation and the National Transplantation Center.

A special contribution in this field has been made by **the Italian company on eye banks** (Society Italian Bank degli Eyes – SIBO), founded in 2000. It is a scientific association that unites the eye banks in the country, located in the respective regions. Thanks to the society, an organization has been created for the exchange of experience and knowledge between specialists in the field of transplant medicine, which in turn improves the quality of the service provided. The main goal of the organization is to support the spread

and improvement of the quality of corneal transplantation and the treatment of eye pathologies by promoting and developing eye banking. The association promotes research activities, the organization of courses, conferences, meetings, seminars and other research initiatives for eye banking and transplantation.

There are 14 banks registered with the National Transplantation Centre in Italy (Fig. 4, Table 1). The Venice Eye Bank Foundation is a non-profit organisation founded in 1987 by Prof. Giovanni Rama and started operating in 1989 as a regional centre for corneal transplantation in the administrative regions of Veneto. and Friuli, located in North Italy. This one ocular bank is in the frontal rankings by number of corneas collected and distributed in Europe, with around 5,000 each year. In addition, the Venice Eye Bank is among the first centres in the world capable of distributing flaps from stem corneal cells, reconstructed in vitro for treatment of eye pathologies that cannot be cured by corneal transplantation alone. The bank supplies corneal material to more than 200 ophthalmological medical centers located on territory on whole Italy, as and supplies with corneas for transplant over 20 medical centers outside Italy (25, 100, 105-107). The Venice Eye Bank also produces transplants from patients' own stem cells. The procedure requires the preliminary collection of stem cells from the patient's eye by biopsy, their cultivation them in laboratory conditions for period from 15 to 20 days and the grafting them in the patient's eye. The Piedmont Cornea Bank was established in 2001 and is located at the City of Health and Science University Hospital. The bank distributes both corneal material and amniotic membrane for transplants. The Rome Eye Bank distributes and corneas and amniotic membrane. In the region on Lombardy function two eye banks. One is the Pavia Eye Bank, which has been operating since 1997, and the second is the Monza Eye Bank, which opened its doors in 1998. The two structures work closely together and manage to provide a large amount of material for transplantation in numerous medical centers in Italy. In addition, banks send donor material in poor and needy hospitals in other countries, when local and national needs for donor material are met.

Fig. 4. Distribution on eye banks in Italy

Table 1. Tissue banks in Italy with authorization to perform corneal and/or amniotic membrane transplantation

Bank	City/ region	Cornea and AM	Only cornea	Only AM
Corneal Bank "Emilia Romagna"	Bologna	X		
Regional Center for corneal grafts	Kozenza	X		
Regional eye bank	Fabriano	X		
Aquila Eye Bank	Aquila	X		
Piero Perelli Corneal Preservation Center	Luke	X		
Cornea Eye Bank Rome	Rome	X		
Branch of Rogovichna Banka Emilia Romagna	Imola	X		
Cornea bank	Barry		X	
Melvin Jones Eye Bank Foundation	Genoa		X	
Veneto Eye Bank Foundation	Mestre		X	
Monza Eye Bank	Monza		X	
Naples Eye Bank	Naples		X	
Eye Bank "Lions of the Sicilian Region Francesco Ponte"	Palermo		X	
Cornea bank of the Piedmont region	Turin		X	
Foundation " Ophthalmology " bank F. Trimarchs', Pavia	Pavia		X	
Amniotic fluid bank membrane of the Piedmont region	Cuneo			X
Bank for fabrics of the Veneto region	Treviso			X

Italy ranks among the first in Europe in terms of the number of cornea donations and transplants performed in ophthalmology. Corneal banks in Italy are evenly distributed throughout the country, which is a prerequisite for both distribution and transplant operations to be accessible throughout the territory.

SPAIN

Transplantation and donation in Spain are mainly regulated by **the Transplantation Law 30/1979 and Royal Decree 2070/1999** . It is noteworthy that under the Spanish legal system, living donation is permissible not only between relatives and emotionally related people, as is the requirement in other European countries, but also between people who do not know each other, provided that the donation is made altruistically and without coercion. In cases of donation, in which a person donates to a complete stranger with the sole purpose of improving the health and quality of life of the recipient, it is necessary for the donor to undergo a series of procedures to ensure that the donor's motive is altruistic, including psychological assessments, reports from social workers, questionnaires, questioning of the donor about his/her work, financial, personal and family circumstances, etc. Consent for "living donation" is required to be expressed before a civil status judge. The validity of consent is linked to the prior provision of detailed information on all the consequences and repercussions that could arise from the donor's decision to donate organs, tissues and cells. From a legal point of view, the validity of consent is the most important aspect of "living donation", since the removal of an organ from a healthy person can be considered a serious crime, according to art. 149 of the Spanish Penal Code. According to art. 156 of the same legal act, exemption from liability is provided in cases where the donor has given free, valid, conscious and expressed consent before the competent authority. The requirements for the donor are: to be legally competent and to be clinically healthy. The Transplantation Law 30/1979 defines the basic legal framework regarding the donation and transplantation of human organs. The law establishes principles that provide legal certainty and guarantee

that the donation process is based on ethical norms and that the fundamental rights of the donor are respected.

The main principles set out in the law are: unpaid donation – for therapeutic purposes only; confidentiality; limitation of advertising of donation. The law also guarantees the anonymity of the donor's recipient, as this requirement supports the principle of confidentiality, as one of the principles governing the entire donation and transplantation process. In addition, the requirement for recipient anonymity is also enshrined in art. 7 of the Spanish **Law 41/2002 on patient autonomy** .

The Transplantation Law 30/1979 contains only seven points, most of which refer to the relevant regulation for each specific activity.

Another fundamental document in the field of donation and transplantation in Spain is **Royal Decree 2070/99** , which was promulgated due to scientific and technical advances in the diagnosis of brain death and the preservation of organs for transplantation. Regarding living donation, the law defines the requirements that must be met in order for the donation to take place. The Royal Decree establishes certain ethical principles on which the donation of organs, tissues and cells is based, creates rules for the coordination of organs, tissues and cells between Spanish regions.

Spain is worldwide leader in the sphere on transplants on organs, fabrics and cells. The state has and highest donor activity in worldwide scale. The Spanish program for donation and transplantations is built on various initiatives and reforms, with the country introducing the creation of specialized institutions in this field, expanded donation criteria, developing strategies for donation in children, ensuring the presence of a coordinator in intensive care units, and the country also uses methods for identifying potential donors in places other than intensive care units. The coordinators have undergone specialized training, which aims to provide basic communication skills, especially those, necessary for family consultations with relatives and close ones on the potential donor (29).

The Spanish strategy in the field of donation includes building

public trust and confidence in the current ones policies in the area on transplants, as and training on health professionals with communication skills to support and encourage donation among the population in donor situations where there is a need for rapid action and decisions. Efforts to train professionals with communication skills in the field of family consultations with relatives of the potential donor, are from essential meaning. The significant success in the field of donation and transplantation in Spain is also due to the three-tier governance structure that Spain has introduced, covering the national, regional and local levels. This includes both the National Transplant Organization and and institutions, dedicated on donation and transplants, which is support at national, regional and local (hospital) level. Spain implements both public and private training for all healthcare personnel involved in donation and transplantation. The National Transplant Organisation, which operates at national level, is responsible for developing a common national strategy in the field of donation and transplantation of organs, tissues and cells, supports cooperation between stakeholders and facilitates the implementation of relevant regulations and guidelines. The National Transplant Organisation is the state technical body under the Ministry of Health, which coordinates the logistics of transplantation and provides 24-hour information for healthcare professionals, providing information on clinical protocols and legal regulations in the field of donation. At regional level, Spain maintains 17 regional offices, which reflect the distribution of donor material in the autonomous regions. The regional offices support the processes on strategic reforms and coordinate transport of organs and tissues. At the local level, Spanish donation hospitals operate. They include medical sisters and doctors, often with experience in the intensive medicine. They are specifically trained for the role you in coordination on the donor activity on hospital level. The task It is up to these individuals to train other hospital staff members, identify potential donors, yes evaluate the medical fitness for donation, yes document the donor activity, consult with relatives and coordinate the entire clinical pathway of donation. According to studies, this three-tier governance structure

in the field of donation is considered there is main contribution for success on Spanish model. This three-stage The device has also been adopted by other countries, including Italy and Portugal, which are developing successful organ, tissue and cell donation and transplantation programs.

An integral part of the Spanish organ, tissue and cell donation and transplantation program is the national quality and comparative analysis system, led by the National Transplant Organization. Hospitals are subject to external inspection, and donor transplant coordinators working in the respective hospitals periodically collect and report a set of indicators of donor activity. The data is reported for development on the local coordination in hospitals, more specifically for everyone independent region. In this way, it is possible to compare donor and transplantation activity in different regions and to emphasize and develop strategic national reform in those in need. is regions. These actions from country on the national coordination are a valuable opportunity to obtain feedback on donor activity and are further evidence of the drive to ensure quality and transparency in the Spanish organ, tissue and cell donation and transplantation program.

A key element that favors donation in Spain is the reimbursement of all costs related to transplantation – the payment of personnel, equipment, as well as all other aids, instruments, medications necessary to perform the transplantation . Hospital budgets include specific funding for organ, tissue and cell donation, based on the activity of the previous year.

The Tissue Bank in Barcelona, Spain is an internationally renowned multi-tissue bank operating in highly qualified staff. The bank controls entirely the process by transplantation, including the identification of potential donors, the collection of the material, as well as its processing and storage. The bank processes all types of tissues. One of the main goals of the Barcelona Tissue Bank is to carry out research, innovation, development, and the development of ideas to improve the public services it provides . The bank is public and operates under the Ministry of Health of Catalonia. The governing body is the Council on the directors, which is consists of

from independent faces with various duties within the institution. The Barcelona Tissue Bank provides a huge variety of tissues, including cornea and amniotic membrane for the goals on ophthalmology. The fabric bank distributes a brochure to inform people about the possibility of donating a placenta. The placenta is the organ that develops during pregnancy , and the amniotic membrane is the innermost layer of the placenta. The amniotic membrane is used as a transplant due to its antimicrobial, anti-inflammatory and regenerative properties. According to the brochures available on the bank's website, the latter distributes three products made from amniotic membrane. The first is a fragment of amniotic membrane placed on nitrocellulose paper, available in two sizes. The second product is an extract of amniotic membrane obtained by lyophilization. It is available in a vial that needs to be dissolved in water according to the instructions. It is applied on the principle of "eye drops". The third product is a fragment of lyophilized amniotic membrane, available in two standard sizes, as well as on order – in a specific size, for the patient's needs. All three products are stored under different temperature conditions, with their application being assessed for each specific case and the specific needs of the patients.

In Europe exists and organization with voluntarily membership – European Association on eye banks (EEBA – European Eye Bank Association). Two of the Bulgarian medical institutions are members of it, 1 bank and 1 user. There is countries in EU, which have no membership (75).

NETHERLANDS

In The Netherlands acts **Law for donation, in force from 31.07.2018** It is set out in the principle for presumed consent for donation for the faces over 18 - year old age. On all citizens is provided opportunity yes register the choice you in a national donor registry, with each person being able to choose from 4 options, namely: consent to donation, non-consent to donation, a decision that the family or partner should take after death on registered, or indication on specifically a person who is authorized to make a

decision about donation. According to the same law, every foreign citizen who has resided in the country for more than three years must register his choice in the national donor register. For convenience and as a reminder, every citizen who has reached the age of majority receives a letter from the donor register asking him to enter his choice, by replying on the letter or by registering the desire you through the website of the donor registry. In cases where there is no explicit choice, any adult who dies in an intensive care unit can be a potential donor. Consent from relatives and loved ones is not required. on the deceased. The latest have law yes object against the donation, but on them the evidentiary burden lies burden yes argue and substantiate the circumstance, that the deceased face did not want to be a postmortem donor. It is noteworthy that the Netherlands applies more extensive criteria for donation than other European countries, as the country allows persons over the age of 12 to be registered in the national donor register. In the event of the death of a registered person between the ages of 12 and 16 and the opportunity to donate his organs and/or tissues arises, his parents or guardians must give their explicit consent before the donation is made. According to statistics at the beginning on 2023 Mr. more from two third from population on Netherlands is registered their choice in the national donor registry, with almost half of those registered having expressed their explicit consent to be donors after their death.

Another important regulatory act is **the Human Tissue Quality and Safety Act** , which specifies the details regarding the receipt, processing, storage and distribution of donated organs and tissues. The Ministry of Health determines competent authorities to be responsible for the legal compliance of the donation procedure and subsequent activities related to transplantation, as well as appointing authorities to inspect accredited institutions and medical facilities. According to Dutch legislation in banks for organs and fabrics is appoints employee, which observe compliance on established rules and monitors the results of safety and quality control tests. After a positive final assessment by the specially designated responsible person in the relevant organization, the

stored tissues and organs can be distributed to the medical institutions where transplants are performed. It is interesting that in the Netherlands transplants can only be performed by university hospitals. Donor tissue, of which there is no shortage and a constant supply is maintained, is provides immediately on the medical restaurants, as such is for example the amniotic membrane. The donor fabric, from which there is shortage, as for example ocular corneas, is officially and legally defined as “distributable.” This tissue is distributed by specially established institutions according to various criteria, including: the urgency of the medical condition, specific criteria for the patient and the tissue regarding their compatibility.

Each organ and tissue bank in Netherlands must yes received accreditation from the competent authority – Ministry of Health. Inspection of all banks is carried out every two years by specially appointed inspectors of the Ministry of Health. The distribution of organs and tissues is carried out by the Netherlands Transplant Foundation, which is also accredited according to the above requirements.

In the Netherlands, there is also a special eye bank in Rotterdam, which is registered as an organization. with non-profit goal and is specialized the activity you in provision only on tissues for eye transplants, both corneas and amniotic membrane. Receiving an eye cornea for transplantation requires that recipients are registered in the database of the Dutch Transplant Foundation. Receiving amniotic membrane only requires filling out a form, as this tissue is kept in constant supply. The eye bank is a member of the European Association of Eye Banks. It is accredited by the Dutch Ministry of Health, Welfare and Sport. and sports, as a bank that meets all statutory requirements under the Bodily Materials Act. The Eye Bank in Rotterdam holds a license to export amniotic membrane and corneal tissue to countries both within and outside the European Union, and in addition has a contract for provision on tissue materials for ocular transplants on clinics in Germany. Thanks to innovative technologies used by the bank for processing donor material, it is possible to use a unit of donor material for more than one transplant.

The criteria for donation have also been expanded due to the fact that new research shows that even people suffering from sepsis at the time of their death can be donors on cornea without contraindication and danger from dissemination on the infection on the recipient.

3. Identification on the medical restaurants with status on "woven" bank and users of eye tissues, according to the registration with the Medical Supervision Agency and quantitative analysis of activities related to eye transplantation in authorized medical institutions based on a survey among specialists involved in these activities

Eye and tissue banks are institutions established for the purpose of collecting, processing, processing, storing and distributing donor materials for transplantation. They certify the suitability and safety of the material, ensuring the traceability of documentation related to donors, tissues and recipients in accordance with current legislation and confidentiality conditions.

To moment on territory on Republic Bulgaria, according to the register on IAMN, There are 6 medical institutions operating with a permit for the collection, processing, storage and distribution of tissues in ophthalmology, presented in Table 2.

Table 2. Medical restaurants with permit for taking, processing, storage and tissue distribution in ophthalmology

Medical facility	Populated place	Permission for	Document number	Active functioning
UNIVERSITY MULTIPROFILE HOSPITAL "N.I.PIROGOV" EAD	Sofia	Collection, examination, processing, storage and provision of bone-tendon, corneal and other tissues for transplantation	No. 19 / 21.12.2010	Yes C, AM
UNIVERSITY MULTIPROFILE HOSPITAL FOR ACTIVE TREATMENT "ALEKSANDROVSKA" EAD	Sofia	Expertise, processing, processing, storage and corneal transplant and amniotic membrane	No.8 / 16.12.2010	NO
UNIVERSITY MULTIPROFILE HOSPITAL FOR ACTIVE TREATMENT "SANTA MARINA" EAD	Varna	Collection, examination, processing, storage, transportation, provision and transplantation	06 / 20.09.2018	NO
SPECIALIZED HOSPITAL FOR EYE DISEASES - VARNA LTD	Varna	Collection, examination, handling, processing, packaging, labeling, storage, transport, provision and - transplantation of tissues (cornea, sclera and amniotic membrane) and cells (limbal stem cells)	SB- 108 / 22.01.2021	
"INTERNATIONAL" EYE TISSUE BANK SOFIA LTD	Sofia	Collection, examination, labeling, processing, transportation and storage for the purpose of providing eye corneal tissue for transplantation	TB- 442 / 10.10.2023	
TISSUE BANK "BIOREGENERACIA" LTD	Sofia	Collection, examination, processing, packaging, labeling, storage, provision and transportation of sclera, cornea and amniotic membrane	RZ-2 / 28.08.2015	Yes C, AM

Each institution is duly registered, for which it holds a permit (the number and year of which are indicated in the table) issued by the competent authority. Of the listed in the table registered

medicinal restaurants four function and carry out activities related to the collection, processing, treatment, storage and distribution of tissues for eye transplants. The consumption of material from eye banks in Bulgaria is not evenly distributed on territory on Republic Bulgaria. This is so, because three from functioning banks are concentrated in city Sofia and only one from them carries out activity outside the capital, in the city of Varna.

The Pirogov Tissue Bank is the first institution in Bulgaria, which began activities in the collection, processing, treatment, storage and distribution of corneal tissue in 1998, and in the years the activity is carried out in different structures on the hospital. Through 2010 d. the existing to that one moment "Department" by preservation on fabrics" to Pirogov University Hospital and Medical Center has received the necessary permission for the collection, examination, processing, packaging, labeling, storage, provision and transportation of corneal tissue for transplantation. The unit still exists today, but its functions are declining.

The International Eye Bank began its operations in 2006, and it is the only tissue bank bank on territory on Republic Bulgaria, which is specialized the activity you only in the field of corneal tissue. Its permit was renewed in October 2023.

"Bioregeneration" is the largest tissue bank in Bulgaria. It began its operations in 2005, introducing numerous innovations and applying modern methods and technologies in its activities. The bank has a permit for collection, examination, processing, packaging, labeling, storage, provision and transportation on corneal fabric for transplantation since 2013. "Bioregeneration" is the only tissue bank in the Republic of Bulgaria that is a member on The European association for tissue and cellular banking (EATCB). Fabric Bioregeneration Bank operates in the form of a commercial enterprise, more specifically a sole proprietorship with limited liability, whose capital is owned by a non-corporate legal entity - the Bioregeneration Foundation.

Through 2014 Mr. in city Varna, as part from the ambitious program on Medical University - Varna, a Center for Translational Medicine and Cell Therapy has been opened at the University Multi-

profile Hospital for Active Treatment (UMBAL) "St. Marina". A Corneal Tissue and Sclera Bank was also established at the Center for Translational Medicine and Cell Therapy in 2021. This is the first eye bank established outside the city of Sofia in the transplantation history on Republic Bulgaria. The meaning on this one center is historically, as it is currently not functioning.

The expertise is transferred in other managed from MU-Varna medicinal establishment, a namely: "USBOBAL-Varna" Ltd., which functions actively from 2021 Mr. The fabric bank is newly registered as a department/unit of the hospital and has permission to collect amniotic membrane, cornea, sclera and limbal stem cells. This makes it the bank with the broadest portfolio of all banks operating in Bulgaria.

Currently, there is no national eye bank or national tissue bank operating in the Republic of Bulgaria. Amniotic membrane in Bulgaria is provided only by three of the above-mentioned banks, a namely: Fabric bank "Pirogov", Fabric bank "Bioregeneration" and the Eye Bank department of USBOBAL-Varna EOOD. Regardless of the registration regime, in Bulgaria there are 3 eye banks operating in the capital and one in Varna (Fig. 5).

Fig. 5. Map of eye banks in the Republic of Bulgaria, 6 registered , of which 4 operating

In the area on corneal transplant in Republic Bulgaria activity by provision of corneal material are again carried out by the four banks, namely: Pirogov Tissue Bank, International Eye Bank Sofia, Bioregeneration Tissue Bank and the Eye Bank Department of USBOBAL-Varna EOOD. Theoretically, according to medical data, in the case of corneal transplantation in a settlement far from Sofia, the

risk of primary rejection of the grafted corneal material could increase, since its transport time is extended, respectively, the viability of the transplant material is reduced.

To moment on territory on Republic Bulgaria, according to the register on IAMN, There are 28 medical institutions operating with a permit to perform cornea, sclera, amniotic membrane and/or stem cell transplantation in ophthalmology, presented in Table 3.

Table 3. Medical institutions with a permit to perform corneal, sclera, amniotic membrane and/or stem cell transplantation in ophthalmology

N	Medical facility	Inhabited place	Permission for	Number of the document	Actively functioning
1	UNIVERSITY MULTIPROFILE HOSPITAL FOR ACTIVE TREATMENT "ALEKSANDROV SKA" EAD	Sofia	Examination, processing , processing, storage and implantation of cornea and amniotic - membrane	No. 8 / 16.12.2010	C, AM
2	UNIVERSITY MULTIPROFILE HOSPITAL FOR ACTIVE TREATMENT "SANTA MARINA" EAD	Varna	Collection, examination, processing, storage, transportation, provision and - implantation of cornea, amniotic membrane and sclera	06 / 20.09.2018	NO
3	SPECIALIZED HOSPITAL PO EYE DISEASES FOR ACTIVE TREATMENT – VARNA LTD	Varna	Tissue collection, examination, processing, packaging, labeling, storage, transportation, provision and transplantation (cornea , sclera and amniotic membrane) and cells (limbal or stem)	SB-108 / 22.01.2021	C, AM, LSK
4	MILITARI MEDICAL ACADEMY – A MULTI - PROFILE HOSPITAL FOR ACTIVE TREATMENT SOFIA	Sofia	Tissue grafting from human cadaver – cornea , amnion, skin and bone-tendon tissue	SG. No. 22 from 10.03.2023	AM

5	MULTI-PROFILE HOSPITAL FOR ACTIVE TREATMENT "SANTA ANNA" AD	Sofia	grafting : cornea and other tissues (sclera, amniotic membrane)	13 / 03.08.2016	AM
6	UNIVERSITY MULTIPROFILE HOSPITAL FOR ACTIVE TREATMENT "PROF . DR. STO JAN KIRKOVYCH AD	Stara Zagora	Grafting on eye cornea, amniotic membrane and sclera	No. 10 / 11.09.2015	AM
7	UNIVERSITY MULTIPROFILE HOSPITAL FOR ACTIVE TREATMENT "DR. GEORGI STRANSKI AD	Pleven	Grafting on eye cornea and others tissues (amniotic membrane)	14 / 13.09.2016	C, AM
8	UNIVERSITY MULTIPROFILE HOSPITAL FOR ACTIVE TREATMENT "QUEEN JOANNA" – ISUL" EAD	Sofia	Grafting of fabrics: Cornea and amnion	2 / 08.02.2016	C, AM
9	ACIBADEM CITY CLINIC, UNIVERSITY MULTIPROFILE HOSPITAL FOR ACTIVE TREATMENT " TOKUDA" EAD	Sofia	Grafting on the cornea and amniotic membrane	MB-311 / 26.06.2023	C, AM
10	MULTI-PROFILE HOSPITAL FOR ACTIVE TREATMENT"SANTA CLEMENTINA" TREATMENT – SOFIA EAD	Sofia	Cornea, sclera grafting and amniotic membrane	5 / 30.06.2014	AM
11	SPECIALIZED EYE HOSPITAL FOR ACTIVE TREATMENT "DR. "TASKOV" Ltd.	Targovisht is	Transplantation on fabrics: sclera and amniotic membrane	SB-351 / 05.11.2021	AM
12	SPECIALIZED EYE HOSPITAL FOR ACTIVE TREATMENT – " ASSOC.PROF GEORGIEV" EOOD	Varna	grafting : cornea and other tissues (sclera, amniotic membrane)	47 / 30.12.2010	No

13	OUTPATIENT – MEDICAL CENTER FOR SPECIALIZED MEDICAL CARE "SANTA PETKA" LTD	Varna	Grafting of fabrics: cornea and other fabrics (sclera, amniotic membrane)	5 / 28.03.2016	C, AM
14	SPECIALIZED EYE HOSPITAL FOR ACTIVE TREATMENT " VISION" LTD	Sofia	Cornea, sclera grafting and amniotic membrane	27 / 22.12.2010	C, AM
15	SPECIALIZED EYE HOSPITAL FOR ACTIVE TREATMENT "ACADEMIC PASHEV" EOOD	Sofia	grafting : cornea and other tissues (sclera, amniotic membrane)	14 / 17.12.2015	C, AM
16	SPECIALIZED HOSPITAL FOR ACTIVE TREATMENT BY EYE DISEASES "ZRENIE" LTD	Sofia	grafting : cornea and other tissues (sclera, amniotic membrane)	26 / 22.12.2010	C, AM
17	SPECIALIZED HOSPITAL FOR ACTIVE TREATMENT BY EYE A R E Y O U SICK "ZORA" LTD.	Sofia	Cornea, sclera grafting and amniotic membrane	UD-00- 2 / 10.01.2019	C, AM
18	SPECIALIZED HOSPITAL FOR ACTIVE TREATMENT BY EYE DISEASES "DEN" LTD	Sofia	grafting : cornea and other tissues (sclera, amniotic membrane)	72 / 25.11.2011	C, AM
19	MEDICAL CENTER "PENTAGRAM 2012" LTD	Sofia	grafting : cornea , etc. ocular tissues (sclera , amniotic membrane)	5 / 24.09.2012	C, AM
20	MEDICAL CENTER OPHTHAL MOLOGY "RESBIOMED " Ltd.	Sofia	Tissue grafting : cornea	7678 / 31.07.2023	C
21	SPECIALIZED EYE HOSPITAL FOR ACTIVE TREATMENT – "PENTAGRAM" LTD.	Sofia	grafting : cornea and other eye tissues (sclera , amniotic - membrane)	1 / 11.01.2013	C, AM

22	ANDREEV OPHTHALMOLOGY MEDICAL CENTER And KO" Ltd.	Sofia	grafting : cornea and other tissues (sclera, amniotic membrane)	7 / 06.06.2016	C, AM
23	SPECIALIZED EYE HOSPITAL FOR ACTIVE TREATMENT - BURGAS LTD	Burgas	grafting : eye cornea and other tissues (sclera, amniotic membrane)	12 / 26.07.2016	AM
24	OUTPATIENT CENTER – MEDICAL CENTER FOR SPECIALIZED MEDICAL CARE – EYE MEDICAL CENTER "ST. NICHOLAS" LTD.	Varna	Grafting of tissues: amniotic membrane	1847 / 13.02.20 23	AM
25	OUTPATIENT – MEDICAL CENTER FOR SPECIALIZED MEDICAL CARE "EYE CLINIC SVETA PETKA" AD	Varna	Grafting of fabrics: cornea and other fabrics (sclera and amniotic membrane)	1882 / 12.07.2023	C, AM
26	"EYE MEDICAL CENTER HASKOVO" LTD.	Haskovo	Grafting of amniotic membrane	1041 / 03.05.20 23	AM
27	"MEDICAL CENTER" EYE LASER " CENTER VISION" LTD.	Sofia	grafting : cornea and other tissues (sclera, amniotic membrane)	28 / 29.04.2005	C, AM
28	SPECIALIZED HOSPITAL FOR ACTIVE TREATMENT OF EYE DISEASES PROSPERITAS Ltd.	Sofia	Transplantation on fabrics and cells: cornea, amniotic membrane, sclera	SB- 443 / 28.03.202 3	C, AM

There are 28 medical institutions that perform transplantation in Bulgaria and they are unevenly distributed as follows: 17 in Sofia, 6 in Varna and one each in Stara Zagora, Pleven, Burgas, Haskovo, Targovishte. The distribution is demonstrated in Fig. 6.

Fig. 6. Geographical distribution of medical institutions performing transplantation in Bulgaria

From the above table and figure it is clear that the distribution is very uneven with dominance on medicinal restaurants, which carry out transplant in the capital, and less from half of the medical institutions distributed in the rest of Bulgaria.

Of the medical institutions, 8 have the status of a “medical center”, with 3 having both a medical center and a hospital registered. This is important from the point of view of the lack of possibility of using a clinical procedure for transplantation in outpatient care. There are 5 medical institutions that function as an independent medical center, without association with a medical institution for hospital care, and the question arises about the mechanism by which the state covers the costs of transplantation in these cases. Only medical institutions for hospital care can benefit from the clinical pathways financed by the NHIF for transplantation in ophthalmology, and the registration of new hospital institutions at the time of preparing the dissertation is practically impossible, due to the factual and political situation in the country. All medical institutions listed in the table, except for one, are registered for amniotic membrane transplantation. There are 3 medical institutions that are registered only for amniotic membrane transplantation. The portfolio of "USBOBAL-Varna" EOOD is the widest.

The survey, distributed among specialists, was completed by 4 managers and 8 employees of eye banks, 6 managers and 37 doctors from 23 medical institutions. It provides information from all operating medical institutions performing transplantation activities.

Of the eye banks, three carry out activities related to the

processing, processing, storage and distribution of amniotic membrane, three – processing, storage and distribution of cornea, with one bank also carrying out processing, two carry out activities related to the processing, processing, storage and distribution on limbal stem cells. Interesting is the fact, that in banks, activities are carried out by an almost equal number of doctors and biologists, which outlines a low fundamental interest in eye banking at the national level.

All specialists by ocular diseases, participating in the survey, are with internship over 2 years and perform a transplant on amniotic membrane. Only 5 specialists with internship over 5 years perform corneal transplantation and only two perform limbal stem cell transplantation. The economic indicators and the attitude towards them from a managerial perspective vary extremely very between the medical restaurants. For 4 from them the activities by the transplant are many important from economic and image-related point of view point, for the rest are no very important or unimportant. The leader in amniotic membrane transplantation is "USBOBAL-Varna" EOOD, with transplantation activities accounting for over 20% of the hospital's activities.

The analysis of the results of the survey conducted shows that practicing physicians who carry out transplants in the area on ophthalmology, and the others specialists, working in healthcare facilities, find regulatory obstacles that negatively impact the implementation on ocular transplants, which obstacles can yes be summarized in 5 groups, namely :

1. lack on regulation for processing of fabrics;
2. legal impossibility for the decision to donate organs and tissues postmortem to be expressed personally by the individual during his or her lifetime, regardless of the wishes of his or her relatives and loved ones;
3. absence of an algorithm for action in donor situations and lack of specific training in the field of communication skills of donor coordinators appointed in medical institutions;
4. insufficient financing on the activities by transplantation;
5. lack on law for organic products.

The main legal obstacle is the lack of clear and legally regulated rules for the processing of ocular tissues and their conversion into a biological product and/or medical devices. There is interest in products with propagated stem cells, but also The two tissue banks with potential cite the "legal vacuum" as the main obstacle to their activities.

It is interesting to note that in Bulgaria, doctors performing transplantation activities have an average age of 42. Considering the small number of corneal surgeons, the age deviation towards to 55 when it comes to corneal transplantation. All doctors, performing transplantation, have at least 1 course/training for the special ones activities, which they carry out. The specialists, participating in the work on tissue banks, have minimum 3 training. Most surgeons obtain material from more than one eye bank, even if the bank is part of the hospital. The average annual number of transplants is 16, with some surgeons performing over 200 transplants. on annual base. The surgeons manifest low interest to the normative regulations, while the rest of the eye bank employees, mainly those working in the field of administration and technical cooperation, are well acquainted with all the laws and regulations in the field of donation and transplantation.

4. Collection, summary and analysis on the information from public registers for the eye tissue transplants performed in Bulgaria and in leading is European countries for the last 10 years

Corneal transplantation in Bulgaria dates back to 1939, when Academician Pashev made the first attempts to transplant a human cornea into an eye with a severe chemical burn, for regret with relatively disappointing results (108, 109). Through the period of "socialism" corneal transplantation with "fresh corneal tissue" is actively performed. In Bulgaria the first ocular bank was established in 2006 Mr. by academician Petya Vasileva, in the period of accession on Republic Bulgaria to The European union. From then to the present There are currently five tissue banks that provide corneas and other tissues, such as sclera, limbal stem cells cells and amniotic membrane. Independently from the European trend for using organ

cultures at +28-37 ^{0}C, corneas in Bulgaria are stored by all banks in transport environments at +2-8 ^{0}C (mainly Optisol). For difference from this, the methodologies for AM preservation methods are quite diverse and include cryopreservation in glycerol, DEMEM or lyophilization. There are no long-term statistics and analysis of tissue use in Bulgaria, and the national Executive agency "Medical" supervision" supports open register from 2020 on its page (https://www.youtube.com/watch?v=1//iamn.bg/en/transplantations /statistics – fabrics – and -cells). However, Bulgaria is part of EUROCET, where since 2012 there has been data on transplants from European countries (https:// www.iss.it/ en/eurocet-data).

From the results in part 2 on the questionnaire study can yes is concluded, that AM is offers mainly from two banks, and cornea from three, with medical institutions directing to the banks on a territorial basis. In order to analyze the trends in transplantation on a national scale, public information summarized by IAMN and EUROCET was used. The results from IAMN are presented in Table 4.

Table 4. Eye transplants, carried out from medicinal restaurants in Bulgaria with fabrics from local eye banks

Year	Cornea	Corneo-scleral - linen button	Sclera	Amniotic membrane	Total
2024 (1st quarter)	43	5	0	86	134
2023	160	10	0	376	2023
2022	90	4	1	421	2022
2021	98	0	1	331	2021
2020	132	0	1	433	2020

After the collection of the available data on AM transplantations from EUROCET, a serious discrepancy was observed, mainly because a different data collection mechanism was used during the collection – in some years the information was based on the number of transplants performed, and in other years – in square millimeters of transplanted product. For the purposes of the analysis in the development, the area of the transplanted material was recalculated

by dividing it by 3.24 as, which is the usual size of the transplant – 1.8/1.8 mm. Another problem was the missing data for Bulgaria in EUROCET for 2013, due to this circumstance the analysis was performed for the period 2014 – 2023 (one year discrepancy of the corneal tissue). The results are presented in Fig. 7.

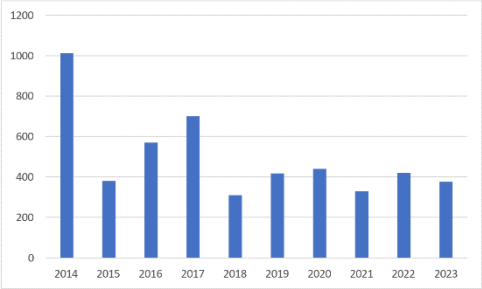

Fig. 7. Transplantation on AM in Bulgaria on the base on register EUROCET and the register of the Executive Agency for Medical - Supervision for a period of 10 years (2014 – 23)

For difference from the transplant on AM, the data for corneal transplant they look much more precise because of the circumstance, that for them is leads strict accountability. This is owes on the fact that corneas is receive from dead body donor and are only 2 in number. For them is leads mandatory documentation and the number on the tissues by the Bulgarian legislation is maximum the number on donors multiplied by 2. Here why fluctuations no is observe. The results in the two the register coincide and are precise, as presented in Fig. 8.

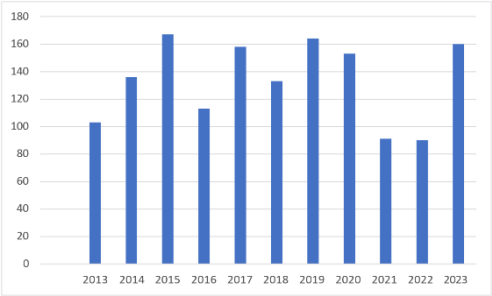

Fig. 8. Corneal transplants, registered from Bulgarian ocular banks by data of EUROCET for a period of 10 years (2013 – 22)

From the information presented, a significant deviation is observed in the donation of amniotic membrane and the number of transplants reported to the relevant registries, and a stable

movement on corneal transplant between 100 and 165 annually, as lowest are the results for the two years of the COVID-19 pandemic.

EUROCET's annual reports cover data on transplants performed in a number of European countries of organs, tissues and cells, including cornea and amniotic membrane. There is some differences in the reporters countries, However, Bulgaria is a consistent participant. It is important to note that for AM in some years the published information is based on the number of transplants, and in other years – as squared centimeters. For to be comparable data, a recalculation was performed, as It is assumed that a single graft is 3.24 cm^2 and the area was divided by this number. Unfortunately, for some periods the information is incomplete and the missing information affects the entire analysis.

Since in 2015 the agency also began collecting information on imported and exported fabrics in and outside EU, was done additional analysis, for yes is evaluate the complex process on exchange tissue, which has always been a hot topic in organ and tissue donation. Since the corneal tissue was donated postmortem, additional analysis was performed on a population-based basis in individual countries.

The quality on the collected data was additionally analyzed, for yes is about prices the reliability of the information. Descriptive statistics were used for the statistical analysis.

Information on AM is provided only in the tissue transplantation section. After collecting the available data on AM transplantations, a serious discrepancy was observed, mainly because during the collection in some years the data were based on the “number” of transplants performed, and in other years – in square millimeters of AM transplanted. A correction was made according to the methodology described for Bulgaria in the previous section. The obtained data on amniotic membrane are shown in Fig. 9.

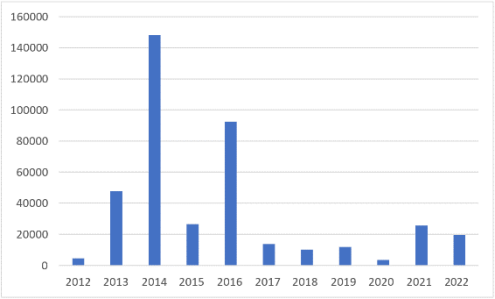

Fig. 9. Number provided amniotic membranes in the Europeans countries on based on the EUROCET register for a period of 10 years (2013 – 22)

The dynamics on the results, which demonstrates the upper figure, probably is owes on missing information.

The results of corneal tissue donation appear to be more accurate. Over a 10-year period, according to the registry, 526,550 corneal transplants were recorded in Europe. Their distribution is shown in Fig. 10.

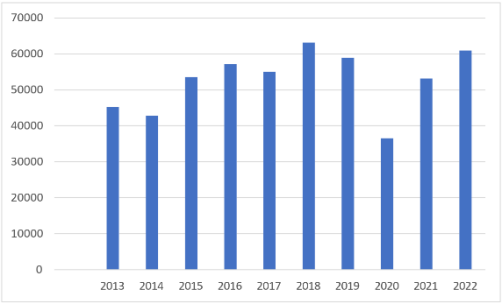

Fig. 10. Transplantation on cornea, provided in European countries, EUROCET reporting for a period of 10 years (2013 – 22)

The trend of the lowest results for the two years during the peak of the COVID-19 pandemic is also observed globally for all European countries.

5. Research on legal barriers and the reasons for the low donor activity and formulation on a work algorithm facilitating awareness among the population about the need for donation

The global shortage of organs and tissues requires that the search for suitable donors be expanded outside the national borders on the countries, as for this one goal are created a number of organizations whose goal is to facilitate and enable the exchange of

organs and tissues between countries.

Cross-border exchange of organs is one very good opportunity for optimal spending of the donor material. Since the beginning of 2019, the Republic of Bulgaria, through the Executive Agency "Medical" supervision", is part from platform for assistance on cross-border exchange of bodies. The name of the platform is FOEDUS, and its goal is to provide fast and effective exchange on information regarding the lack on suitable or needy is patients at the national level, or in cases of searching for organs for patients who are in a life-threatening condition. Activities related to transplantation are carried out in accordance with the national regulations of the receiving and offering country, as well as in accordance with supranational European regulations.

The FOEDUS platform began operating in 2012, continuously expanding its scope. The platform's activities stem from the intended in Directive 2010/53/EU text, according to which the exchange on organs between Member States of the European Union is a way to increase the number of available organs and to ensure better compatibility between donor and recipient. The platform operates 24/7, but only European national transplant organisations have access to it. In the platform is register suggestions for available organs, which no can be used for transplantation in the country of origin, as well as requests for necessary organ at urgent situations. In case that is find suitable recipient in other a member state of the European Union, with priority given to patients in need from member states of the FOEDUS, or suitable organ for urgently needy is patient in countries, which no are members of the organization, the facilitated, thanks to the functioning FOEDUS platform, is applied and on explicitly the intended in the area European regulation, process by cooperation to carry out organ exchange.

In the development for analysis on export and import on fabrics in the area on ophthalmology is The EUROCET registry, which is a European registry for organs and tissues, funded by a European Commission program, was used, the purpose of which is to create, collect and update data from Member States in the field of organ, tissue and cell donation, as well as transplantation activities. The

registry is discussed in detail in point 4 of the tasks set in the dissertation.

In 2015, EUROCET started reporting on import/export of organs and tissues. Due to the fact that this is a significant issue for the development, an analysis of the data provided in the field of ophthalmic transplantation was also carried out, and in particular on imports. and export on cornea. Through 2015 Mr. the biggest importer on corneas from the countries from EU is Spain (223 corneas), and from non-EU countries is Cyprus (65 corneas). At the same time, the three countries, the largest exporters of corneal tissue, are Italy (488 corneas), followed by the Netherlands (256 corneas) and France (254 corneas). In 2015, the total number of corneas imported was 924, and the number of corneas exported was 1764. The situation changed in 2016, when the leader in corneal imports was Germany (1244 corneas, 90% from non-EU countries). Italy was the largest exporter in the same year (533 corneas). Through 2016 total number of corneas imported is 3624, a total exported – 5830. Through 2017 Mr. the trend is the same, as again the largest importer is Germany (984 mainly from non-EU countries), and the largest exporter is Italy (652 corneas), as total imported corneas are 1591, and exported 1691. For 2018 Mr. no is a significant change was noted with Germany taking the lead in imports (1377 mainly from non-EU countries) and Italy as the main exporter (750 corneas – 29% for non-EU countries), but with a significant presence as exporter and on Netherlands (605 corneas – 12% for countries outside EU). For the same year, the total number of corneas imported was 1711, and the total number of corneas exported was 1786. In 2019, Germany imported 848 corneas, mainly from non-EU countries, and Italy exported 619 corneas – 34%, to non-EU countries, followed by the Netherlands (605 corneas, 12% to non-EU countries). The total exchange imported corneas is 2671 and exported – 1986. For 2020 Mr. Germany is contributed 1100 corneas, mainly from non-EU countries, and Italy exported 791 corneas – 26%, to non-EU countries, followed by the Netherlands (422 corneas, 10% to non-EU countries). The total number of corneas imported for 2020 is 2271, and exported – 1716. For 2021, the largest importer is again

Germany (1116 corneas, mainly from non-EU countries), and the exporters are Italy (913 corneas – 29%, to non-EU countries) and the Netherlands (620 corneas – 7% to non-EU countries). The total number of corneas imported is 1556, and exported – 1991. And for the last published year – 2022, the trend is the same, with Germany importing 808 mainly from non-EU countries, Italy exporting 904 corneas – 42%, to non-EU countries, and the Netherlands – 568 corneas – 8% to non-EU countries. The total number of corneas imported for 2022 is 1243, and the total exported is 1885. Imports of tissues for ophthalmic transplantation are mainly from non-EU countries and are largely carried out by Germany (Fig. 11), while exports are mainly within the European Union, with Italy and the Netherlands leading the way, with Italy distributing slightly more corneal material outside the EU (Fig. 12).

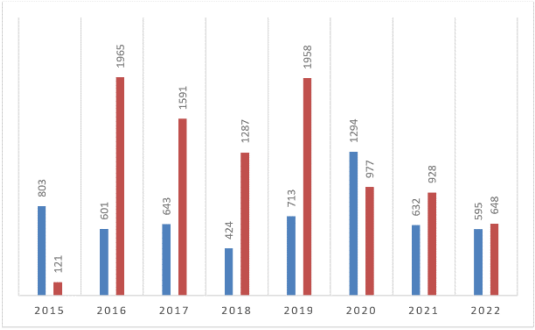

Fig. 11. Imports of - corneal tissue into EU - countries , based on EUROCET data for an 8-year period (2015–22). Blue columns – imports from EU countries, orange – imports from non-EU countries

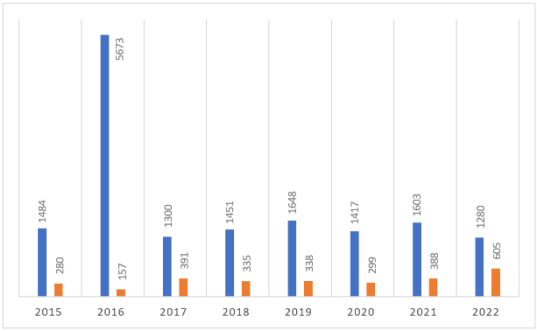

Fig. 12. Export on corneal fabric from the countries from EU, on basis on data on EUROCET for a period of 8 years (2015 – 22). Blue columns - and exports to EU countries, orange - exports to non-EU countries

The profound analysis on the national healthcare in the leading

countries in the area on The imports of corneas, namely: Germany, followed by Spain, show that both countries have very well-functioning health systems that cover all the costs of transplantation and subsequent treatment for their citizens. This in turn allows the waiting list of patients for transplant yes be significantly smaller on head from population in compared to other European countries, including the Republic of Bulgaria. On the other hand, from a legal point of view, the import of corneas into Bulgaria is practically impossible. This statement is supported by the fact that there is no legal payer for these tissues. A study conducted shows that the cost of importing a cornea is about 5,000 euros, and the amount that the Ministry of on healthcare reimburse through clinical path for transplant of a cornea, is only 1250 leva. By law, the balance, which exceeds several times the amount that the state reimburses, cannot be paid by the patient, since the Transplantation Act of organs, tissues and cells explicitly commands, that The transplant is free for the patients, and more specifically – Art. 5 on the same law prohibits the organs and the tissues yes be the subject of a punitive transaction. In this regard, importing corneas would be a violation of the law. The analysis on the data from the register EUROCET shows, that leaders in the area on export on corneas are Italy and the Netherlands. Both countries export corneal material mainly in member states of the European Union, with Italy also distributing fabrics to countries outside the Union. On the territory of the Republic of Bulgaria, the export of corneas is also not applicable due to legal restrictions regulations, and more specifically - from Article 37 on ZTOTK, according to which export on fabrics and cells intended for transplant in third countries, is performs after satisfaction The needs of the Republic of Bulgaria. The constant and growing list of patients in need of corneal transplantation thwarts the possibility of the Republic of Bulgaria being an exporter of cornea. Studies have shown that people are inclined towards charity, but despite This practice proves that they are strictly reserved to donation of "eyes". On the other hand, the country has the potential and opportunity to be an exporter, and accordingly to offer to the European market another tissue applicable in eye transplantation, namely - amniotic

membrane.

Improving communication between medical professionals and coordinators working in hospitals, from one country, and the potential donors and their loved ones, from other country, is a strategic and necessary step in the process of overcoming the shortage of donor material. Spain is one of the countries whose leadership positions in the field of donation are due precisely to expert communication, based on excellent communication skills, active listening, and the ability to ask questions. Achieving complete clarity in this communication is question on experience and observations. Requires is the conversation with the potential donor and his/her relatives to be conducted by competent, calm, and dedicated specialists. Mediation techniques would could yes set the frame, which must yes is follows at discussion of a donor situation. Dealing with emotions and empathy are seen as key mediating methods, which together with the active listening are directed to creation on an overall atmosphere of security and trust, and towards building working relationships between the coordinator of the medical facility and the relatives and/or loved ones of the deceased person – a potential donor. Part from the mediators techniques would could yes be successfully applied when conducting on the conversations with these faces. The reason for this is, that for yes is the decision is lawful for donation as on the potential donor, so and on his/her loved ones, must yes is entirely voluntary in nature. The role of the specialists who communicate with these people is mainly to explain in an accessible and understandable language the altruistic nature of donation, its therapeutic advantages for recipients, to show empathy and understanding for the delicate moment in which the potential donor and his relatives find themselves. The donor coordinator must be active in the entire communication process, applying masterful techniques characteristic of mediation, concerning the ability, even with silence, to help the relatives and friends of the potential donor to share what is important to them and the deceased circumstances, yes urge these faces yes arrange you think you, as cooperates even by the ton on the voice you or with appropriate expression and suitable words for this,

yes gave reverse connection, that he has understood exactly the words said, the emotions expressed, but on the other hand he must maintain impartiality and neutrality and not interfere in the decision of the relatives and friends by giving a specific answer or exerting influence or coercion on the decision to donate. Coordinators should not convince and urge the relatives and friends of the deceased to make a specific decision, their role is to establish an empathetic dialogue so that the latter are accessiblely informed and supported at this delicate moment. Specialists and/or coordinators who are assigned to medical institutions should not exert influence through verbal pressure on the final solution for donation, so as this circumstance would meant violation of the fundamental principle of voluntariness, which accompanies the entire process of donation and transplantation and is enshrined in the Law on Transplantation of Organs, Tissues and Cells. A basic principle in the application of mediation techniques is that the donor coordinator appointed in the medical institution should yes is neutral and impartial expert, which there is the skills yes extinguishes tension, to clarify the controversial issues, interests and needs of the parties. The role of the "mediator-coordinator" is to guide the conversation, through various and specific mediation methods, to help the potential donor and his relatives to independently assess the positives and negatives of possible solutions and to choose the most acceptable and informed solution according to their own views and understandings. The mediation procedure is characterized by relative speed, since making an urgent decision is of crucial importance in the field of donation and transplantation. In cases where the potential donor is not registered in a national donor registry, in which he has explicitly declared his refusal to become a donor after his death, the decision to donate organs and tissues is on his/her close ones and relatives. Despite the accessible national registers and/or donor cards in most European countries, their role is more informative about the potential donor's wishes, rather than probative force, and although in some cases registration has been made in due order in such a register, with a expressed wish for the person to become a postmortem donor, or the possession of a donor card, practice

shows that in most cases the final decision belongs of relatives and the relatives of the deceased face. Possible is the last yes have as different opinion between you regarding the decision to donate organs and tissues to the potential donor, even if they are not fully familiar with the donation and transplantation procedure and the nobility of this act. The limited time after death on the potential donor, through which the organs and the tissues his are suitable for transplantation, requires specific skills and speed on the part of medical specialists and coordinators working in hospitals who conduct conversations with the relatives of the deceased person at this delicate moment. Appropriately presented information is decisive for making an informed decision. Empathetic communication, characteristic of mediation, there is their own specifics, as requires very attention, sense and understanding. Achieving understanding refers not only to the emotions, but also to the thoughts and experiences of the potential donor's relatives, and the requirement is that they receive information about this understanding. Having an empathetic conversation is also a skill that would help the coordinator by donation, which conducts the conversation, yes understand emotions, the circumstances, the intentions, you think and needs on relatives on the deceased face, so that yes can yes offer sensitive, understanding and appropriate communication and support. The basic principles of mediation should be the guiding principles in conducting these conversations. The principle of voluntariness is characteristic of both mediation – participation in a procedure or conversation with a specialist/coordinator must be entirely voluntary – and is a fundamental and statutory principle in the LTTA, relating to the entire donation and transplantation procedure. The principle on equality, characteristic and for mediation, can yes found application in cases where the relatives of the deceased have different opinions among themselves regarding the donation of organs and tissues of the deceased person - a potential donor. This principle is expressed in the equal opportunities of each party - close to the potential donor, who is authorized and legitimated to make a decision regarding donation, to present their opinion, statements and

arguments. The guarantee of this principle is also based on the observance of other principles in mediation, according to which the donor coordinator has the obligation yes be neutral and impartial. The principle on confidentiality, characteristic of both mediation and all procedures concerning donation and transplantation, again regulated in The law for transplant on organs, fabrics and cells, is widely used both in conversations and communication between the coordinator of the medical facility and the relatives of the potential donor, as well as in cases of subsequent donation and transplantation.

The first stage is the identification of a possible donor , during which the competencies of the staff of the medical institutions and, more specifically, medical specialists are valuable - doctors, which have skills and knowledge yes identify possible donor. On At this stage, several essential elements should be taken into account, namely:

- possible donor can yes be only deceased in medicinal establishment person;
- the possible donor must yes be in advance evaluated on base age, cause of death, diseases, medical history;
- the coordinator by donation follows yes plans contact with relatives of the deceased.

In the multidisciplinary hospitals for actively treatment there is departments, in which there is multiple "possible donors", which requires specific work with the staff of the medical institutions. The work of the donor coordinators is extremely difficult, and taking only a corneal fabric is exceptionally unattractive activity and from economic point of view point. Mediation techniques should be directed at actively working to obtain corneal tissue from every possible donor.

The second stage is determination on potential donor , as in this one moment from paramount The skills of donor coordinators to conduct full and detailed communication are important with relatives on the potential donor. On this one stage are important the following circumstances:

- potential donor can yes be only transferred in department by

pathology;

- the potential donor must yes be in detail evaluated for contraindications for donation;
- the eye status must yes be analyzed through inspection and review on the documentation;
- The donation coordinator must contact the deceased's relatives.

This is the most essential element of the algorithm, since the development of the potential donor situation depends on its outcome. Of paramount importance is the information provided by the donor coordinator to the relatives and friends of the potential donor due to the fact that In Bulgaria there is a tendency to refuse to take corneal tissue due to the fact that the relatives are left with the impression that the orbits will remain empty. Even when taking a whole eyeball (which is not allowed in the Republic of Bulgaria) the orbit is prosthetic and the eyelids are fixed in a closed position. This circumstance requires an adequate explanation by the coordinator and provision of accessible and understandable language on the information, that the taking on fabric no yes violate the facial appearance of the deceased person – a potential donor.

As a result from held conversation and the taken from the entitled relatives and/or close ones decision is made, the third stage is reached **, involving actions in relation to the identified donor** . From one country, this one stage includes actions, for which competent and responsible is the coordinator on donation – filling out documents: declaration-consent for donation from the relatives of the identified person donor, documents for postmortem care, at necessity others notifications, reports, notifications. On the other hand, actions within the competence of medical specialists, doctors and laboratory technicians are carried out - medical examinations and samples from the identified donor, if necessary other tests. When implementing the third stage - actions in relation to the identified corneal tissue donor, the following elements are essential:

- consent on the entitled close ones or relatives for donation on corneal tissue, given in writing in due course;
- taking on blood samples for serology and others research;

- readiness on the team by explantation on corneas;
- readiness of the eye bank for processing and storage processes of donations woven material.

Mediation techniques of empathy and sympathy at this stage can be applied again to the relatives and friends of the identified donor, in connection with the difficult task of documenting their consent and filling out other blank documents that follows yes be attached to the file on the donor. Psychological support can be offered to doctors who have chosen the field of ophthalmology, as this specialty in the medical profession there is famous remoteness from death and the doctors who practice it have psychological barriers that need to be overcome.

The fourth stage concerns actions concerning the actual donor . These include, on the one hand, follow-up by the donor coordinator of the relevant medical facility, compliance with the formal country on clinical procedures, compliance on the order, movement and sending to the competent authorities of the necessary documentation, and on the other hand, proceeding to the explantation of the relevant organs and tissues of the real donor, carried out by the relevant medical specialists. At this stage of the procedure, the implementation of the following elements is important:

- availability on negative mandatory serological samples;
- lack on medical contraindications, including and reporting of exactly time after death occurs;
- explantation on corneas and their immediate assessment;
- transportation on the tissues to ocular bank.

At this stage, the coordinator at the medical facility must monitor compliance with and documentation of all statutory and regulated procedures, as well as the sending of the necessary documents to the competent authority. Due to the nature of the situation and the need for rapid action, teams may make documentary omissions that could vitiate the donation procedure and the subsequent transplantation be thwarted.

The fifth stage is the realized donor , which stage is again the

result of coordination between the donation coordinator at the medical facility and the medical specialists. On the one hand, the doctors in the relevant medical direction must yes identify potential and real recipients, a from other country, the coordinator by donation yes notify recipients to find a donor and perform the transplant. At this stage, the following elements need to be considered:

- corneal fabric is successfully transported to eye bank;
- done is macroscopic, biomicroscopic and speculative assessment on the fabric;
- confirmed is the negative serology;
- The eye bank makes decisions about processing and/or distributing the tissues according to the waiting list.

Mediation techniques at this stage can be directed at the appropriate recipients, who can be informed in a favorable manner about the possibility of an upcoming transplantation. In Bulgaria no serious religious and/or social obstacles for accepting donor tissue, but there are psychological ones. The work of donation coordinators with potential recipients, as well as the provision of accessible and understandable information for them about the subsequent care that they need to take for their health, especially in a certain period after the surgical procedure, is a guarantee for improving the chances of a successful transplant.

The developed algorithm is schematically presented on Fig. 13.

Fig. 13.
Schematically presentation on the developed algorithm

All stages on the procedure by donation and the subsequent transplant require good verbal and communication skills both between specialists in medical facilities, employees in the specialized institution that coordinates, documents and registers all transplants on territory on Republic Bulgaria – Executive "Medical Supervision Agency ", as well as with the relatives and/or close friends of potential donors. This communication requires the persons holding the position of "donation coordinator" in medical institutions to possess, on the one hand, specific communication skills, and on the other hand, knowledge of the terminology covering both medical activities and legal requirements in the country, in order to ensure compliance with both clinical and medical requirements and legal provisions.

6. Look in the future – legal and ethical aspects on donation and the transplant in Bulgaria

Essential task on the study is yes present current review on the national systems in different European countries in the field of donation and transplantation, to compare strategies and the policies on the countries. The development goals yes is establish useful practices and to summarize valuable information needed for countries to learn from each other to identify ways to build better programs for donation and organ and tissue transplantation. The dissertation aims to develop a conceptual framework of the best strategies and tactics that can be adopted both at the national and European levels.

The increase in donor activity is a consequence of diverse factors that some European countries have successfully implemented. Spain, as a leader in the field of donation and transplantation, can serve as a model for countries with lower donor activity. activity, in this number and Republic Bulgaria, which is orders on one from the last places in this classification. Countries that set themselves the goal of reforming their policies in the field of donation and transplantation, should compare their strategies and policies with those of countries with high donor activity, to identify

useful practices and to summarize the valuable information they need to learn from each other to identify ways to build better organ and tissue donation and transplantation programs. Deriving a conceptual framework of the best strategies and tactics from the Spanish model should yes be placed as priority for the rest countries, so as this one valuable and a time-proven comprehensive Spanish system, as well as the information derived from its operation serves as a basis and working sample. As a result on The above-mentioned highlights of the current Spanish model can be synthesized in several directions:

- specialized institutions – three-stage structure on management, which covers national, regional and local levels;
- quality assurance processes – the national quality and benchmarking system, led by the National Transplant Organization, including external inspection of medical facilities and donation coordinators;
- detailed cost recovery schemes – reimbursement of all costs, related with the transplant, by plan, prepared on basis on the previous year's accounts;
- comprehensive training programs – specialized qualification of healthcare professionals to acquire communication skills to support and encourage donation among the population;
- population awareness – close cooperation with the media and conducting publicly accessible campaigns aimed at informing the country's population about the need for donation;
- expanded criteria for donation – Spanish legal system admits donation between people who do not know each other, provided that the donation is made altruistically, without any profit motive and without the exercise of coercion.

Countries that aim to reform their programs should track and study periodic quality assessments, reporting, and feedback as vital strategies, which can yes be developed and successfully applied, for yes provide continuous improvement in the area on donation and the transplant. In In addition, the example of a country like Spain illustrates that efforts to strengthen primary care and improve

primary, secondary and tertiary disease prevention should be seen as integral components of any donation program. and transplant on organs. Investments in these areas can yes relieve the high demand for organ transplantation worldwide. In addition, the Spanish experience has been published in the national governmental register. (Ten Lessons From the Spanish Model of Organ Donation and Transplantation - PMC (nih.gov).

The promotion of donation in Spain is also linked to campaigns conducted to inform the general public about the need for this act of generosity and nobility. The practice shows, that the people no are familiar neither with the real one shortage on organs and tissues worldwide, nor do they have detailed information about the nature of the procedure. The neglect by national governments of the importance of providing accessible information about donation and transplantation to the population is one of the factors that prevent countries from increasing their donor activity.

This study identifies a critical link between donation, transplantation and their financing, which is one of the fundamental problems in Bulgaria. It would be appropriate to establish a mechanism in Bulgarian legislation to recalculate the real value of all activities related to donation and transplantation, as well as their reimbursement. The development of this statement also has political implications, as it is necessary for politicians to review the social significance of each aspect of transplantation and to identify all moral, social, legal and financial barriers. Donation is priceless act, but the costs on the preparation, collection, storage, processing and distribution of tissues and organs has progressively growing price. In Bulgaria the activities by ocular transplant are lowest paid compared to other organ and tissue transplants. Eye banks have a stated cost of 3000 BGN per unit of corneal tissue, and the reimbursement is only 1250 BGN. The stated costs of eye banks are calculated from the sum of the costs for coordination, the labor of the bank employees, materials, long-term tangible assets, the need for continuous updates, and administrative activities.

The increase in donor activity may be linked to the possibility for

individuals to yes can independently during life yes express preferences you for donation, regardless of the wishes of their relatives and friends. The presumed consent for donation implemented in the Netherlands works better than that provided in other countries, including the ones studied in the present development, on first look same regime, according to which each A person who has not explicitly registered his refusal to be a postmortem donor in the national donor register is considered to be such. According to practice and legal provisions, however, the final decision of a person to be a postmortem donor is be a donor, except in cases of explicit disagreement, is taken by the relatives or friends of the deceased. In the Netherlands, the possibility is provided for the relatives or friends of the deceased person - a potential donor who did not declare his preference during his lifetime in the national donor register - to oppose the donation, but in this case it is their responsibility to present evidence that this was the actual will of the deceased person. Practice shows that after the introduction of this system, donor activity has increased significantly. It would be appropriate in the Republic of Bulgaria to establish a mechanism by which every person during his lifetime can independently objectify his choice to be a donor after his death in a document that has legal value.

The proposed algorithm for improving communication through the use of mediation techniques and approaches at each stage of possible or existing donor situations, presented in detail in Task 5 from the present labor, there is for goal improvement on communication between donation coordinators in medical facilities and authorized relatives and friends of the potential donor, in order to make an optimally quick and informed decision.

The policies for reformation on the national systems for transplant must yes are based on long-term commitments and strategies for achievement on sustainable success. The European Countries seeking to develop or reform their national programs should work on building a similar culture of trust and transparency, as this is essential for gaining the trust of the population and maintaining high levels of organ and tissue donation.

Considering the difficulties for suggestions for political reform and as part from solution on the last one placed in the development, for active "look" in the future" was taken decision to develop an information brochure for the general audience, to be made available to suitable language with the role on the transplant on cornea and amniotic membrane to rescue on vision on needy is patients. The brochure is used in public campaigns in 2023 and 2024 (Fig. 14).

Fig. 14. Brochure for improvement on public awareness for the role of donation to protect eye health

CHAPTER FOUR. DISCUSSION

The basic law, which regulates in detail the process of carrying out transplantation in the Republic of Bulgaria, is the Transplantation Act of organs, tissues and cells (ZTOTK). In the field of postmortem donation (lat. Postmortem), according to the provisions of the same law, in Bulgaria is applies so-called principle for the presumed consent, according to which is perceives, that any person who has not explicitly expressed their unwillingness to donate during their lifetime, for the purposes of transplantation, organs, fabrics or cells from his/her own body, is agree yes be dead body donor after his death. The law has also regulated the hypothesis according to which the assumption introduced is possible from the law, yes no answers on the actual will on the deceased the face. Therefore, in the current legal framework, as a condition for performing posthumous explantation of organs, tissues and cells for the purposes of transplantation, in Art. 21, para. 1, item 3, ZTOTK, mandatory notification of the deceased's relatives, arranged by law in four lines, and waiting on reasonably short deadline, in which relatives can yes do written refusal for donation. The above-mentioned period within which relatives can express their disagreement with donation is not precisely regulated in the legal norms, but it is recommended to be reasonably short in order to preserve the function of the organs in the event of organ explantation. In the event of refusal by the relatives of the deceased person, it should not be motivated. In the practice imposed in Bulgaria, in the absence of a written refusal, before proceeding with explantation, it is accepted as an additional condition to apply an explicit written consent for donation on organs, fabrics and cells, done from relatives on the deceased person.

In Bulgaria, there is an official register at the Executive Agency for Medical Supervision, in which every person during their lifetime has the right to express their disagreement with being a donor of organs, tissues and cells. after his death. To date, as of Since the establishment of the register, less than 3,000 people have registered their refusal to be postmortem donors. The procedure for entry into the register includes submitting a form to the IAMN, as the legal basis

for entry in the register is Art. 11, para. 5, so on 3, ZTOTK. Provided is opportunity for submitting the application both on site at the Administrative Service Center of the IAMN and through the portal for providing electronic services. It is possible to submit the application using the services of a licensed postal operator. The Minister of Health is the body that exercises control over IAMN, as the agency creates and maintains the aforementioned donor registry, in accordance with legal provisions.

According to statistically data Bulgaria borrow last place in transplanted patients on 1 million people, from all 28 member states of the European Union. In Europe, the number of patients waiting for a suitable organ or tissue also exceeds the number of transplants performed, although the growth in donation is higher than in Bulgaria. The present study rejected the claim that Bulgaria is in last place in terms of transplant activity in the field of ophthalmology. It turns out is, that for 6.45 million, which is 1.4% from the European population, for 10 - year period, Bulgaria is registered 22 198 corneal transplants, which is 4.2% from all eye transplants in Europe. This is a significant achievement and shows that corneal surgery in Bulgaria cannot be compared with the number of transplants performed in France, Spain and Italy, but is far above the European average. The results of this study also showed the following trends:

- unevenness in the processing on amniotic membrane in Europe and Bulgaria;
- probable regulatory and registration imperfections, especially in some M e m b e r States ;
- shortage on corneal material in Bulgaria and Europe;
- more non-Community import (mainly from USA) and smaller percentage export (mainly to Africa) of corneal material;
- need from optimization on corneal processing with goal receiving on more tissue products from one donor.

Supranational legal regulation and the transposition her in the Bulgarian legislation

The supranational legal framework defining standards for organ, tissue and cells, is exposed in Directive 2004/23/EC on European

Parliament and on Council from 31.03.2004 on the establishment of quality and safety standards for donation, supply, control, the processing, storage, storage and the distribution of human tissues and cells, called in legal parlance the European Directive on tissues and cells, and in Directive 2010/45/EU on The European parliament and on Council from 7.07.2010 d. on standards of quality and safety of human organs intended for transplantation. The directives set out the quality standards and safety for the organs, such as are covered all steps in the process on transplantation, including, but non-exhaustively, the following are detailed: donation, delivery, control, processing, storage, distribution. The Directives are transposed in the Bulgarian legislation from August 2012 d. through The law for transplant on fabrics, organs and cells (ZTOTK), The law for health, The law on medical institutions (LZH) and the relevant existing or newly introduced by-laws, namely: Ordinance No. 1 of 26.03.2019 on the conditions and procedure for carrying out inspections by the Executive Agency "Medical Supervision"; Ordinance No. 6 of 16.03.2007 on approving a medical standard for transplantation of organs, tissues and cells; Ordinance No. 7 from 28.8.2012 for the requirements for the qualification and health status of persons who carry out the collection, examination, treatment, processing, labeling, storage and transplantation of organs, tissues and cells; Ordinance No. 10 of 15.05.2007 on the conditions and procedure for notification, registration, reporting and transmission of information on serious adverse reactions and serious incidents, and for blocking, withdrawal and destruction of tissues and cells; Ordinance No. 11 of 02.12.2011 on the procedure for the provision of eggs, sperm and fertilized eggs, which no are used for creation on offspring, on scientific, educational and medical institutions in the country and abroad for medical, scientific and therapeutic purposes; Ordinance No. 12-A of 12.05.2004 on the conditions and procedure for the provision of organs, tissues and cells that cannot be used for transplantation for medical reasons, for other therapeutic, diagnostic and scientific and medical goals; Ordinance No. 12 from 20.04.2007 for row for establishment and authentication on the circumstances, at which can yes is carried out taking on organs,

tissues and cells from a deceased person; Ordinance No. 13 of 12.05.2004 on the conditions that must be met by the quality of tissues and cells subject to international exchange for the needs of the Republic of Bulgaria; Ordinance No. 21 of 15.05.2007 on the circumstances and data that are entered in the registers of the Executive Agency "Medical Supervision", the procedure for entry and use on the information; Ordinance No.22 from 15.05.2007 for the conditions and row for registration and reporting on the activities of expertise, collection, transplantation, processing, processing, storage and labeling of organs, tissues and cells and for the preparation of annual reports by medical institutions.

At the supranational level, a European system for coding tissue and cell products has been envisaged and developed, which system consists of a register of all types of tissues and cells placed on the market in the European Union and their corresponding product codes. The requirement to provide such a code is explicitly laid down in Commission Directive 2006/86/EC of 24.10.2006 implementing Directive 2004/23/EC of the European Parliament and of the Council of 11 October 2006 on the of the Council on establishing traceability requirements, reporting of serious adverse reactions and events and certain technical requirements regarding coding, processing, storage, storage and provision on human fabrics and cells. The requirement imposed by the Directive has been transposed into the national legislation of the Republic of Bulgaria, in par.1, item 1 of the DR of Ordinance No. 22 of 2007. The purpose of the provided The code is to ensure the correct identification of the donor and the traceability of the donated material, to provide information about the basic characteristics and properties of tissues and cells. In Art. 10 on the quoted one above Directive, concerning The European system for coding, the requirement has been introduced that the code includes at least the information specified in Annex VII of the same Directive. In addition, as on supranational level in the indicated Directive, so in Bulgarian law, in par. 1, item 4 from the Amendment to Ordinance No. 22 of 2007 The requirement for possession of a unique number from a medical institution that is accredited and has the right to carry out tissue and cell transplantation activities is set.

The European Commission cooperates with expert bodies such as the Council of Europe and the European Centre for prevention and control on diseases (ECDC), for yes is guarantees safety and to optimize the use of donor material in the field of transplantation, by developing practical guidelines that support transplant centers and organ procurement organizations in the implementation of the European regulatory framework.

Of particular importance in the field of tissue and cell transplantation, in order to complement and clarify the main one supranational normative act – The European directive regarding the tissues and cells, the following supranational documents, listed in detail below, also apply, offering detailed regulation of various areas in the field of tissue and cell transplantation, namely: Commission Directive 2006/17/EC on certain technical requirements in connection with donation, the delivery and control on human fabrics and cells; Commission Directive 2006/86/EC laying down traceability requirements, reporting of serious unwanted reactions and manifestations and certain technical requirements by attitude of coding, processing, storage, storage and provision on human fabrics and cells; Commission Directive 2015/565 amending Directive 2006/86/EC as regards certain technical requirements for the coding on human fabrics and cells; Directive 2015/566 of the Commission implementing Directive 2004/23/EC as regards compliance control procedures on the equivalents standards for quality and safety on imported fabrics and cells.

In addition, considering the significant progress on biotechnology and the possibility for use of tissues and cells in transplantation, the European Commission prepares reports on the implementation of the legislation, and at the time of preparation of the dissertation the following decisions of great importance in the field of tissue and cell transplantation have been adopted, namely: Commission Decision of 3.08.2010 on the introduction of basic rules on the methods of conducting transplantation provided for in Directive 2004/23/EC of the European Parliament and of the Council on inspections and measures by control, as and regarding the training and the increase of the qualification on employees in the area on

human fabrics and cells; Solution on Commission of 03.07.2015 on the provision of product codes for use in the Single European Code.

The Council of Europe regularly updates the technical requirements in its Quality Guide and safety on the organs for transplantation. The European center for Disease Prevention and Control (ECDC) prepares risk assessments and preparedness plans when there are epidemiological outbreaks related to blood, tissues, cells and organs.

In very European countries amniotic membrane is medical product and/or organic product and can yes is applies intraoperatively, in outpatient conditions and even as drops (1, 52, 61, 64, 66, 69, 72, 110-114). Many of the sources cited distinguish as an advantage the better economic effect at application on the membrane in outpatient conditions. Other very important than legal point of view point aspect is the lack on risks from rejection. Everything again, must yes is take into account the fact that this is therapy with tissue originating from another person and the legal regulation of the entire process mandatory must yes corresponds on medical procedures in the relevant country. The analysis of the EUROCET registry found zero amniotic membrane transplantation in Romania. This is clearly not true, as data show that Romanian ophthalmologists have repeatedly presented data on AM transplantation in Romanian, Bulgarian and international forums (115). Romanian regulations allow for the collection of fresh membrane from a donor with consent for a blood sample. This determines the lack of data for our northern neighbor. Unfortunately, there is still no regulation in Europe that can be used at the European Union level, and this determines the large difference in the data that this study reported in the EUROCET registry. In this regard and in this specific case, the legal reform should cover not only national, but also European legislation.

Information from public registers on eye tissue transplants performed in Bulgaria and Europe

Amniotic membrane transplantation is widely used in ophthalmology, but in recent years a variety of biological products and medical devices have served as substitutes (59, 60, 63, 85, 110).

This probably explains the very limited number of amniotic membrane transplantations in European countries according to EUROCET. In contrast, amniotic membrane transplantation is 3-4 times more common in European countries than in the United States. more frequently performed surgery than corneal transplantation in Bulgaria. The main reason for this trend may be legal, due to the fact that transplantation is fully covered by public funds, while this is not always the case with medical devices and products. Nevertheless, the study in this paper focuses on the missing information regarding transplantations and seamless applications of products derived from amniotic membrane.

The cornea is a transparent tissue with optical properties that provides a sharp, focused image to the retina. When it is not transparent, the cornea causes visual impairment and blindness (116). Among the etiological causes of blindness, including cataracts, glaucoma, refractive errors, macular degeneration, and corneal opacities, depending on the analysis, between 3rd and 5th place (116, 117). Despite that in Africa the most common reason for corneal blindness is trachoma, in Europe the causes are mainly hereditary diseases (mainly corneal dystrophies), trauma and iatrogenic diseases (43). The only way to cure corneal blindness with partial or full thickness corneal transplantation requires donor tissue from an eye bank (117).

The idea for preservation on human cornea is published for first road from Filatov in 1935 (16). After the first created ocular bank in USA quality on the tissues and the procedures for safety are is improved significantly in worldwide scale. The advantages on eye banks include not only regulations and quality control, but also longer storage, in-house preparation, optimization of tissue use and exchange in case of emergency and need, and many other advantages. In Europe, the European Eye Bank Association (EEBA) was founded in 1989 Mr. and in moment includes 27 European countries with over 85 ocular banks. Members of EEBA are more USA, Sri Lanka, Kenya and Australia. In the published literature is emphasizes, that EEBA is a scientific organization committed to developing standards to ensure the best quality among institutions

in Europe. Bulgaria is a member only through one of the banks. The information for Bulgaria highlights the limitations of the legal regulations and the fact that only corneal tissue (corneoscleral button) can be collected for transplantation. In addition, in Bulgaria a potential obstacle to tissue donation is the requirement for permission from relatives of the deceased, regardless of the will of the deceased. Similar problems exist in Europe, as discussed by Sandiumenge et al. (118). The authors trace the possible travel and obstacles from a potential donor to the tissue used and also highlight the missing elements of the pan-European registry. In Bulgaria ocular banking is decentralized and under the aegis on Executive Medical Supervision Agency . Thus, Bulgaria follows the European model and as a result, there are more than 85 eye banks in Europe in 27 member states. EEBA provides relevant information for each individual country, as well as guidelines and standards regarding various aspects of eye transplantation. Despite this, eye banks in each country must yes follow national rules and regulations. In Bulgaria, for example, there is a statutory restriction on extracting the entire eyeball, which reduces the chances of more scleral tissue and examination of ocular structures.

Our study found mixed information on the number of corneal transplants performed across Europe. According to Jones et al., approximately 35,000 corneas are delivered annually using EEBA (75). Based on the study conducted in this paper, based on data from the EUROCET registry, the number is significantly higher, with over 60 000 corneas through 2022 Mr. Obviously this excludes 2020 Mr. because of the pandemic from COVID - 19, but the number on corneas in the register everything more is higher, than in the register on EEBA for 2015 Mr. (119). Considering the number of inhabitants of Europe (448.4 million), there are about 136 donations per million people. This number for Bulgaria, even and for very the active 2023 year, is barely 24.8 on million.

Despite that it seems, that Bulgaria is active in transplants and in the provision on data of EUROCET, donation on corneal fabric is very low, especially as is there is considering the high mortality rate in the country. There are many social, regulatory and medical problems,

which need to be reviewed to improve the situation. It must also be acknowledged that in general the number on the donations on cornea on head from population in Europe is lower from this one in The USA, where donations are over 350 per million, but the median for all countries is 25 per million (120). Therefore, the results for Bulgaria are close to the median and not too bad.

The fact that there are five eye banks in Bulgaria is interesting from a legal and economic point of view. Obviously, this higher population does not increase the number of donations or the interest in this generous act by the public. Moreover, the banks are only in the capital and one large city, which no is good distribution and coverage. Despite that very factors no can to be changed, changing regulations, legal frameworks and public awareness are in the upper part on the list, for yes is facilitate more donations and transplants of the cornea and reduce corneal blindness. Regardless of the future prospects for artificial corneas and ocular surface products, the quality of life of many people depends on the availability of corneal donor tissue. Therefore, tissue donation for potential applications at transplant on eyes, as cornea and amniotic membranes, is a generous act and a gift of sight to other people.

CONCLUSION

Technological progress in the sphere on the products, subject on tissue engineering, in i.e. "tissue-cell allograft product", allows the development and application of biological drugs that have a beneficial effect on the processes of restoring eye health in patients. The lack of legislative framework creates obstacles and an objective legal impossibility for the distribution of such products. Although created in the laboratory, they cannot be put into operation or on the market. This circumstance hinders the possibilities for their application on those in need patients. In this regard, despite the definition of "bioproducts" or the so-called "tissue-cell allograft product" defined in the Medical Devices Act, there is no explicit legal regulation regarding their production, registration, or a dedicated body that exercises control over their production and distribution.

Bulgaria is a small country, but it occupies a worthy place on the European map of corneal transplantation. This does not diminish the problem of corneal tissue deficiency and the long waiting list. The Bulgarian territorial map of transplantation distribution shows significant unevenness with a concentration in the cities of Sofia and Varna. This has adverse consequences in several aspects, namely:

- difficult access to transplant and tracking on transplant patients;
- lack on footage and conditions for development on transplantation;
- increase on number on the people with "corneal" blindness", which is in the group of the "preventable" blindness".

The development of bioproducts and medical devices for anterior ocular surface management would lead to a more even distribution of these medical activities and better access for a large portion of the population, especially in the Northwestern region.

CONCLUSIONS

This work is devoted to the study of the legislative framework in the field of eye transplantation (cornea, sclera, limbal stem cells and amniotic membrane) in the Republic of Bulgaria and other European countries. The specific nature of the specialty "Ophthalmology", as well as the peculiarities of transplantation in a social, medical and legal aspect, create conditions for a complicated interpretation of each individual element of transplantation. Despite this complexity and incomplete normative base, the transplant is opportunity for insurance on vision and quality of life of thousands of patients in Bulgaria and millions in Europe and the world.

From the review and analysis of the regulatory framework of other European countries, the following conclusions were formulated:

- It can be summarized that Bulgaria has a satisfactory regulatory framework regarding the complete process of performing corneal and AM transplantation, and the application of medical devices, but the Bulgarian legal system lacks both a law that would regulate the transplantation of biological products obtained by multiplying cells on a suitable substrate - matrix, for example amniotic membrane, and legal norms that would regulate autotransplantation;
- Legislative changes in line with European directives are needed, as well as the adoption of a Biological Products Act. This is because there is potential for the development of ophthalmic transplantations by processing the patient's own cells into bioproducts and implanting this device into the patient's eye for the purpose of treating and regenerating POPs;
- In order to facilitate the transplantation process and donation, it is possible for the amniotic membrane to be treated as a medical device and a personalized medical device (so-called custom-made medical device). Personalized medical devices are regulated in the Medical Devices Act. The study of the legislative framework in this regard shows that the possibility of proliferated stem cells being treated as a medical device is becoming extremely complicated. Therefore, it is appropriate to introduce changes in the legal

framework that will contribute to the optimization and improvement of these processes;

- In Bulgaria, there is a need for collaborative work between institutions, eye banks, medical facilities and eye surgeons in order to increase transplantation surgery , by improving communication between all structures and personnel who carry out various activities related to donation and transplantation. The laws are general and apply to all medical specialties. Considering the many specificities of eye transplantation, the role of experts and specialists in advisory boards is of particular importance;
- The rapid introduction of new methods for treating POP is important for improving on quality on life and vision on the patients. In Bulgaria there is legal obstacles for taking on solutions from medical tips and consiliums, as and lack a definition of "treatment of last resort", which is established practice in Europe;
- The application of new technologies requires new regulations. Bioprinted and artificially populated tissues with allogeneic and autologous cells are about to be created. Corneal tissue is a unique opportunity for this translational approach. Unfortunately, legislative changes are lagging behind the pace at which medical science is developing;
- The lack of tissues requires liberalization of processing procedures, allowing for greater efficiency. Translational medicine is the future of engineered and artificial tissues and requires legislative changes, allowing the application of new technologies beyond the scope of medical devices . This once again emphasizes the need for a legislative framework that affirms the place and role of biological products.

CONTRIBUTIONS, RELATED With DISSERTATION WORK

As a result of this work, 10 contributions have been formulated, of which three are of a scientific-applied and scientific-theoretical nature and four are of a confirmatory nature.

Contributions with applied science character

- For the first time, a national map of eye banks and eye tissue consumption has been prepared. A comparison has been made with Italy – the European leader in transplantation.
- For the first time, a retrospective comparative analysis of transplantation in Europe has been conducted and Bulgaria's position in this context has been compared. It has been proven that Bulgaria is the carrier of 4.2% of corneal transplantation in Europe, with a population of 1.4% of the European population.
- A special algorithm for the realization of a donor situation and processing of corneal tissue has been created. For the first time, the role and place of the use of mediator techniques in the complex process of transforming a possible donor into a realized donor situation is indicated and specified.

Contributions with scientific-theoretical character

- Done is analysis on legislative regulation, concerning the transplant, medical devices and biological products in the Republic of Bulgaria. The weak points and legislative gaps in the context of eye transplantation and the opportunities in the context of European directives are commented on.
- An analysis of the legal framework regarding transplantation and biological products in Europe was carried out, with a focus on leading countries: France, Italy and Spain.
- Analyzed are the good ones practices on the countries – leaders in eye transplantation in the EU, in the context of regulatory provisions, and their practices for meeting the needs for transplantation, export and import of tissues have been studied

and analyzed.

Contributions with confirmatory

- An analysis of the published literature was conducted and contemporary "good practices" in legislative frameworks at the national and European level were identified.
- The “legislative gaps” and their effects on the rapidly developing translational practice of tissue engineering and bioprinting are analyzed.
- Compared are the advantages on "medical" products", including "custom-made medical devices", with regard to transplants and biological products.
- Made is analysis on the registers to IAMN and "EUROCET" and are established the strong and weaknesses in collecting and publishing public information.

PUBLICATIONS related to the dissertation

1. L. Grupcheva . Study of the legal framework in European countries in the field of transplantation in ophthalmology. *Varna Medical Forum.* 2024, 13 (online first).

PUBLICATIONS

2. Grupcheva, CN; Grupchev, DI; Usheva, N.; Grupcheva, LO . Beauty versus Health—How Eyelash Extensions May Affect Dry Eye Disease? *J. Clin. Med.* 2024 , *13* , 3101. https://doi.org/ 10.3390/jcm13113101
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