ACTIVITIES OF THE SERBIAN BIOETHICS COMMITTEE

Dragoslav Marinković
President of the Serbian Bioethics Committee
Serbian Academy of Sciences and Arts, Belgrade

Professional education in sciences, as well in medicine, had a long history in Serbia. The schools of the highest range, teaching natural sciences and modern medical practice, were established since the middle of 19th century, being headed and organized by specialists who accomplished their qualifications in the highest educational centers in Europe. The practice that leading specialists had to have a specialization in well known medical or scientific centers, has been practiced from the beginning of last century, and particularly applied after the Second World War. Among presently existing ca. 8.000 scientists (half of them being teachers at one of 12 Universities), almost everyone spent substantial period of education in one of well known centers abroad.

Mendelian genetics was thought in Medical Faculty in Belgrade since 1924; genetic counseling was introduced in major clinics since 1960s; full studies of molecular biology started in 1970. Two years before that, i.e. ca. 40 years ago, the Yugoslav Genetic Society and journal Genetika (in English) were established. Five Congresses and more than twenty national and international Symposia have been organized in former Yugoslavian Republics. Criteria are based on publications in well known scientific journals, quality of work is compared with those in foreign laboratories, with which the mutual exchange of visits was frequent. All those criteria, of course, involve the highest ethical merits and principles, which are self-confident when doing scientific research, especially in those fields where human beings are subject of investigation.

A temporal isolation of Yugoslavia in last decade of 20th century produced substantial damages in economical and scientific developments of our country. The newly formed state Serbia and Montenegro became the member of the council of Europe on April 4, 2003, and signed the European Convention on Human Rights soon after. Our national UNESCO commission, as well as Serbian Academy and six State-Universities, have made exceptional efforts to re-establish all connections that existed before 1990s. In SASA we succeeded to re-establish such active relationships with more than 30 foreign Academies, being one of the organizers of cooperation between Academies of SE Europe, based on so called “Venice Declaration” signed in 2001 by 11 Academies from this region, under the patronage of the European Union. Their representatives
meet every year, having ambitious plans for cooperation in different fields of science and culture, among them also in biomedicine. This field is quite strongly developed especially in the Institutes and Universities of Belgrade, Nis and Novi Sad, but also in other medical centers of Serbia.

In October 2003 UNESCO commission of Serbia and Montenegro established its National Committee for Bioethics, consisting of eleven respectful members from Belgrade, Novi Sad, Nis and Podgorica, with the settlement in the Serbian Academy of Sciences and Arts in Belgrade. Some of its members have been involved, since 2002, in final discussions about International Declaration on human genetic data, summarized in UNESCO meetings of IBC and IGBC in Paris in June 2003, contributing to its final form proclaimed in 32nd UN Assembly in October 2003.

Being invited, in 8th COMETH meeting in Dubrovnik in May 2005, to join 29 other National Ethics Committees of the European Council was an exceptional privilege, where we accepted “Convention for the protection of human rights and dignity of the human being with regards to the application of biology and medicine” (Oviedo 1997), as well as its additional Protocols “on the prohibition of cloning human beings” (Paris 1998), “... concerning transplantation of organs” (Strasbourg 2002) and “... concerning biomedical research” (Strasbourg 2004). Accepting the basic principles of this Convention, we feel capable to proceed and apply its rules in the practice of our biomedical research, and to include them in our legislation, i.e. in Laws and Protocols which already exist, or in those that are in preparation. From the spring of last year (2006.), due to the change of the status of our State, our committee changed its name to the National committee for bioethics of UNESCO commission of Serbia. Presently it has 16 members, among them five academicians, eight University professors and three scientific councilors, as distinguished representatives from different towns and fields of bio-medicine.

The basic aim of our Bioethical committee was to strengthen the network of existing Committees in medical centers, in scientific institutes and in Universities, and to help them in accepting the principles from the Convention on human rights in biomedicine of the Council of Europe (1997-2004), as well as from the Universal declaration on bioethics and human rights accepted in 2005 at 33rd Assembly of UNESCO, to be hopefully further improved in 34th Assembly this Autumn in Paris. Meanwhile, we had numerous contacts with bioethical committees of other countries, being actively present, e.g., in a regional conference organized last year in Bucharest, and in IBC meetings in Paris... Our two year activities of broad education of medical practitioners, preceded in Serbia, Macedonia and in Slovakia, were highly estimated at a summarized meeting held in Athens in May 2006, with a perspective to be continued, as a model, also in other European countries.

Last fall, in October 2006, our Committee organized a symposium here in the Serbian Academy, with international participation, entitled “Bioethics in Science and Medicine”. Almost 200 participants were present, and each of them obtained a book with submitted reports, containing broad discussions and advices how to apply practical principles in Bioethical committees in medical and scientific centers. Meanwhile, their activities and application of principles from provided Declarations and Conventions seem to be more emphasized than
before. We applied to our Ministry of health and Ministry of science with suggestions that basic principles of bioethics have to be included in existing laws in these fields. One of the basic principle, that human cloning is prohibited in our country, is now clearly stated in our new Constitution of Republic of Serbia.

This Conference is also one of our efforts to transfer the newest information and ideas that appeared in the field of bioethics to our colleagues from bioethical committees from Serbian institutions, with a privilege that we have here, as our distinguished guests, the members of Bioethical committee of the Council of Europe, who came to help us to exchange our experience, and to come to a conclusion how to further improve our activities in time which is in front of us.

Literature

THE WORK OF THE COUNCIL OF EUROPE IN THE FIELD OF BIOETHICS

Elmar Doppelfeld

Nuclear Medicine, University of Bonn, Germany

1Human Rights and Biomedicine

Council of Europe and European Union

The Council of Europe and the European Union are very often confused even by citizens of states belonging already for some decades to one or both of these groups.

The Council of Europe has been set up in 1949 as an intergovernmental organization. Actually it is composed by 47 Member States covering a population of about 800 millions habitants. Canada, USA, Japan, Mexico and the Holy See are observer states. The intentions of the Council of Europe can be shortly characterized by two illustrating terms “Human Rights” and “Democracy”. In more detail the aim can be described as an achievement of a greater unity between its members and that one of the methods by which that aim is to be pursued is the maintenance and further realisation of human rights and fundamental freedoms in accordance to the title of its “Convention for the Protection of Human and Fundamental Freedoms of 4 November 1950”. This convention is considered as the basis of the whole work of the Council of Europe.

The Council has several institutions to fulfil its tasks (Fig1). The most important institution is the Committee (sic!) of Ministers, composed by the permanent representatives of the Member States, mostly ambassadors. This unit is the leading and deciding body of the Council. The Secretary General is responsible for the whole administration of the Council and for the negotiations between the Council and the Member States and groups outside the Council. The Parliamentary Assembly represents the parliaments of the Member States. The assembly is composed by delegates of the parliaments of the Member States, its members are not directly elected. The assembly should therefore and for other reasons not be confused with the European Parliament. Nevertheless, the assembly is a very important counselling body for the Committee of Ministers. The European Court of Human Rights as institution of the Council can be claimed in cases of assumed violation of human rights.

The Council has different instruments to influence legislation and regulations in the Member States. In first place range conventions and additional protocols as legally binding instruments.

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1 Presented to the Bilateral Meeting within the Framework of the Cooperation Program to Strengthen the Rule of Law (Belgrade, 28 – 29 June 2007): The Council of Europe’s Bioethical Instruments and Promotion of Research Ethics in Serbia
Conventions of the Council of Europe are treaties of the international right and as such follow all conditions of this part of the international legal system. On the basis of a convention additional protocols for a specific scope may be elaborated in the frame of the underlying convention. Conventions and additional protocols need to be signed and ratified by Member States to enter into a legally binding force. Signature and ratification of an additional protocol require that the underlying convention has been already or is signed and ratified in the same moment. Conventions and additional protocols enter into a force as conventions and additional protocols of the Council of Europe if signed and ratified by five states, among them at least four Member States of the Council. Conventions and additional protocols are opened for signature and ratification also by other states than Member States under conditions foreseen in the specific convention.

**Council of Europe**

**Institutions**
- Committee of Ministers
- Secretary General
- Parliamentary Assembly
- European Court of Human Rights

**Instruments**
- Conventions
- Additional Protocols
  
  Legally binding only if signed and ratified by Member State!

- Recommendations to the governments of Member States (non-binding)

Fig. 1.

The Committee of Ministers may adopt recommendations to the governments of Member States on specific fields, for instance research on biomedical material of human origin. Recommendations are non-binding instruments, they may be considered as an advice to states for their internal regulation or legislation.

The European Union (Fig 2), actually composed by 27 member states, representing a population of about 490 millions, has also several institutions. The European Parliament is different to the Parliamentary Assembly of the Council directly elected by the citizens in the Member States. It is more and more included in the decision procedures. The Council of the European Union is the representation of the governments of the Member States. The European Commission at Brussels serves as the leading, but not independent body of the European Union and is entitled to take decisions of binding character.

**European Union**

- 27 Member States (population: about 490 Mio)

  Central institutions:
  - European Parliament
  - Council of the European Union
European Union

The regulating instruments of the European Union are adopted at Brussels by the different institutions and have different binding force. Regulations are directly legally binding instruments for the Member States. They have to be followed as adopted at Brussels starting with the day foreseen in the instrument. Directives may be considered more as a binding framework for national legislation or regulation, leaving special fields to national solutions within the given frame. Member States are entitled to deviate under condition that the aim of a directive is preserved. Guidelines can be characterized as a recommendation for national regulation. The time period for the adoption of a directive is laid down as well as the date of its entry into force. If a state is missing the date of entry into force its citizens may require that the directive is used as adopted at Brussels.

With respect to international treaties like the conventions of the Council of Europe it has to be underlined that the internal legislation of Member States of the European Union has to comply on the base of the right of the European Union with this other treaties.

From the Idea to a Legal Instrument

An idea for a legal instrument may be borne at several places. Members of the Parliamentary Assembly, governments of Member States, members of the European Parliament, the Committee of Ministers, the public or Non Governmental Organizations (NGOs) may propose a kind of regulation for a specific scope. Also Steering Committees like the CDBI² are entitled to present such a proposal. First of all the Committee of Ministers, consulting if

² The abbreviation „CDBI“ is derived from its french name: Comité Directeur pour la Bioéthique”
appropriate other institutions, has to decide on the acceptance of such an idea and to define the legal character of the new instrument. Then it charges the Steering Committee which is competent for the envisaged instrument. This is in the field of bioethics the “Steering Committee on Bioethics (CDBI)”, and the time consuming way from the idea to the instrument will be described in the context to this committee (Fig 3).

First of all the plenary assembly of the CDBI, composed by the delegations of the Member States including representatives of the governments as well as experts, discusses the more general principles of the foreseen regulation. The results of this debate give the frame for the following elaboration of a draft version. Thereafter the CDBI sets up a working party for the preparation of this draft. A working party is usually composed by some members of the CDBI who are considered to be experts on this special field and are familiar with the different steps of procedures of the Council. In addition governments of Member States may appoint as members experts in the field of biomedicine e.g. medical researchers, physicians, lawyers or ethicists. The number of the members of a working party is for financial reasons and with regard to the economy of the work mostly restricted to 6 – 8 persons. They elect a chair, very often a member of the CDBI. The working party sends the first draft and later redrafted versions to the plenary of the CDBI for discussion. Usually after this discussion the paper will be sent back to the working party for reconsideration in the light of the debate and changes if necessary or appropriate. The drafts are opened for discussions so that not only the representatives of the governments within the CDBI, but also the public and the NGOs can comment the text. The Committee of Ministers may consult the Parliamentary Assembly, the European Parliament or other institutions at any stage of the procedure. It should be underlined that representatives of the European Commission and of the Parliamentary Assembly join the debates during the plenary assembly of the CDBI. This participation allows already in a very early stage of the development
of a document to prevent provisions which could be not in conformity with other European regulations. In the case of discrepancies the CDBI tries to find a harmonic solution. By the above mentioned cooperation a doubling of the work of the European Union and the Council of Europe can also be avoided. Finally and at the end of this time consuming, usually some years lasting process like a go and back the CDBI adopts the text of a convention, of an additional protocol or of a recommendation by the two third majorities of its votes as required by the bylaws set up by the Committee of Ministers for Steering Committees. An adopted text is given to the Committee of Ministers. This body may send it for further comments, remarks or even proposals for any change to the Member States, to the Parliamentary Assembly and to the European Parliament. At the end of this counselling procedure the Committee of Ministers decides definitively on the legal character of the new instrument and opens it for signature by the Member States or other States which are entitled to become a party of the instrument.

**Convention on Human Rights and Biomedicine**

The first and until today the most important convention which has been elaborated by the CDBI is the “Convention for the Protection of Human Rights and Dignity of the Human Being with regards to the Application of Biology and Medicine”(1). This convention has been opened for signature at Oviedo/Spain and is therefore also cited as “Convention of Oviedo”.

The title indicates very clearly the aims of this international treaty: the protection of human rights and dignity of the human being with regard to the application of biology and medicine. This rather broad scope covers all fields including medical research and regulates basically the routine work of physicians or other healthcare professionals and the performance of scientific projects. The content of all articles is worded in accordance with this general line.

The aim of the convention is repeated in article 1(Fig 4) with a specific wording by adding the guarantee of respect for the integrity and other rights and fundamental freedoms of the person concerned and the prohibition of any kind of discrimination. Parties to the convention are obliged to introduce into their internal legislation the appropriate measures for safeguarding these principles.

There is some general provisions: Article 2 – Primacy of the Human Being - tries to equilibrate the interests of the individual human being and of the society stating clearly, that the interest and welfare of the human being shall prevail over the sole interest of society or science. Equitable access to health care, as required by article 3, has been criticised as being in a wrong place in such a convention, which is not focussed on the regulation of social and healthcare systems.

**Article 1 – Purpose and object**

Parties to this Convention shall protect the dignity and identity of all human beings and guarantee everyone, without discrimination, respect for their integrity and other rights and fundamental freedoms with regard to the application of biology and medicine.
Each Party shall take in its internal law the necessary measures to give effect to the provisions of this Convention.

The convention requires in article 4, that any intervention in the health field including research has to follow professional obligations and standards. This provision has been discussed for some times as to be too weak in a legal sense. The reason for this criticism was that professional obligations and standards are very often defined by health care professionals. Taking into account, that depending on the specific legal provisions in the Member States, these definitions are adopted under the supervision of the state and given a binding character, the cited wording has been accepted.

The world wide accepted principle of free and informed consent is one of the corner stones of the convention (Fig 5).

**Article 5 – General rule**

An intervention in the health field may only be carried out after the person concerned has given free and informed consent to it.

This person shall beforehand be given appropriate information as to the purpose and nature of the intervention as well as on its consequences and risks. The person concerned may freely withdraw consent at any time.

As article 5 states this free and informed consent is a need for all interventions in the health field. There is no definition of the term “intervention”. It may be understood as physical intervention on the human body as well as any other procedure which may touch the psychological well being of the person concerned. The use of questionnaires for health purposes is the usual example. The information has to be appropriate in the sense of being complete and understandable for the person concerned. The information should also cover the risks if a proposed and justified intervention is not performed. Free withdrawal of consent, allowed at any time, should not exclude the person concerned from other health care measures to which he or she has agreed.

For the protection of persons not able to consent an authorization by a legal representative in accordance with national law is required (article 6). Such an intervention may only be authorized for the direct benefit of the person not able to consent. This provision covers minors as well as adults for a certain time period or for ever not able to consent. For both of these groups in decision making by the representative the opinion or the participation of the represented person to the extent of his or her age, maturity or understanding shall be taken into consideration. Specific regulations for these groups as participants of research projects will be dealt with later.
Subject to protective conditions prescribed by law, including supervisory, control and appeal procedures, a person who has a mental disorder of a serious nature may be subjected without his or her consent to an intervention aimed as treating his or her mental disorder only where, without such treatment, serious harm is likely to result to his or her health (article 7). In emergency situations a physician is entitled to perform immediately without an appropriate consent any medically necessary intervention for the benefit of the health of the individual concerned (article 8). Previously expressed wishes shall be “taken into account” (article 9). This wording reflects the different legal character of the so called “living will” in the Member States of the Council, at least in the period of the preparation of the convention.

There are specific provisions for the protection of private life and the right to information. Everyone has the right to respect for private life in relation to information about his or her health. Every person must be on request informed on any information collected about his or her health. The wish not to be informed shall be observed to prevent any kind of forced information. Nevertheless the law may introduce the right to inform a patient even against his or her wish on findings with relevance for his or her health or for the health of others e.g. the spouse (article 10). The chapter IV “Human genome” contains provisions on non-discrimination on the basis of the genetic heritage, on the restriction of the use of predictive genetic tests only for health purposes or research linked to health purposes, on the prohibition of any kind of intervention on the human genome with the aim to introduce modifications of the genome of descendants and on selection of sex. The articles of chapter VI give the frame for any legislation on organ and tissue removal from living donors for transplantation purposes.

The human body as such may not be a source of financial gain (article 21). A part of the human body, which has been removed, may be stored and used for a purpose other than that for which it was removed only if this is done in conformity with appropriate information and consent procedures (article 22). This is the specific legal condition for requiring free informed consent for the scientific use of any kind of stored biological material of human origin. This provision is an important legal basis for the recommendation on research using such material.

Restrictions of the rights codified by the convention may be placed by law and if necessary in a democratic society in the interest of public safety, for the prevention of crime, for the protection of public health or for the protection of the rights and freedoms of others. Some protective articles of the convention may not restrict under the above cited provision like research on persons not able to consent (article 26). It should be underlined that the convention entitles Parties to it to grant a wider protection for the citizens of that state (article 27). On the other hand no Party is allowed to provide a lower level of protection than given by the convention.

Bioethics is an objective which should interest all groups of society. Therefore Parties to the convention are obliged to facilitate an appropriate public discussion (article 28). A lot of provisions are dedicated to fields which are compulsory for international treaties such as “Interpretation and follow-up of the Convention”, “Amendments to the Convention” or “Final clauses”. The latter
covers e.g. the terms signature, ratification and entry into force. Any state may make a reservation to provisions of the convention if they are not in conformity with the national law. However reservations of a general character are not permitted.

The convention allows concluding additional protocols.

**Article 31 – Protocols**

Protocols may be concluded in pursuance of Article 32, with a view to developing, in specific fields, the principles contained in this Convention.

The Protocols shall be open for signature by Signatories of the Convention.

They shall be subject to ratification, acceptance or approval. A Signatory may not ratify, accept or approve Protocols without previously or simultaneously ratifying accepting or approving the Convention.

These protocols are legally binding instruments for the development of the principles of the convention in specific fields. They may serve as a kind of adoption of the provisions to fields of application like biomedical research. But the frame given by the convention must not be deviated or weakened. The protocols shall be opened for signature only by signatories of the convention. The convention states clearly, that a signatory may not ratify, accept or approve protocols without previously or simultaneously ratifying, accepting or approving the Convention. This provision has been introduced to prevent any kind of “shopping of protocol” without respecting the principles of the underlying convention.

On the basis of this article 31 in the last years protocols on the prohibition of cloning of human beings, concerning transplantation of organs and tissues of human origin, on biomedical research and, recently, on genetic testing for health purposes have been presented. The in 2006 adopted recommendation on research using human biological materials has been prepared also within the frame of the convention. (For more formal details of the work of the Council of Europe in the field of bioethics see Fig 8).

**Scientific research**

Ethics in research is the main topic of the meeting. Therefore the relevant provisions of the Convention, contained in chapter V “Scientific research”, for this field of application will be considered in more details.

The convention underlines as a general rule the principle of freedom of research in biology and medicine. However, this does not mean an absolute freedom. The research has to follow the conditions of the convention and all other legal protective provisions for research participants (article 15).
Fundamental and universally by the scientific community accepted conditions for any research project have to be fulfilled. There is no alternative of comparable effectiveness to research on human beings. This condition has to be examined in the light of possible alternatives like experiments using animals, human tissue or human cells. Methods and procedures of research have to be appropriate in relation to the aim. There has to be a scientific merit of the research project and an important aim. The risks for the participants must not be disproportionate to the potential benefits. This can be explained shortly by the wording “the lower the potential benefit for the participant, the lower the acceptable risk!”

There has to take place an independent examination of the scientific merits of the project including the importance of its scientific aim. A multidisciplinary review of the ethical acceptability of a research project is obligatory. It depends on national regulations which bodies are responsible for the examination and for the ethical review. There are sometimes different bodies for these tasks, sometimes the ethics committee is the competent body for both of them. Only after this examination and after the ethical review a competent body, e.g. an authority, may approve the project if national law requires such an approval (article 16). In some states this approval is obligatory. In other states like Germany an approval of a competent authority is only required for drug trials or for research using X-rays or radioactive isotopes.

The invited participant has to be informed on his or her rights and on the protective safeguards prescribed by law. Of course the necessary free and informed consent as formulated in article 5 (Fig 5) has to be given expressly and specifically. It is repeated that this consent may be freely withdrawn at any time.

In research on persons without the capacity to consent exists the legal obstacle that a legally valuable consent by the person concerned cannot be obtained. A legal representation is therefore necessary. There is a need for research on this group, which may be composed e.g. by newborns, minors, unconscious victims of accidents or diseases or persons suffering from a form of dementia like Alzheimer’s disease. This research can be justified by the fact that a better understanding of the conditions and an improvement of health care in these situations can only be achieved by research on these groups. Research on adult healthy volunteers e.g. cannot reveal the different states of development of the newborn hip by ultrasound. A basic research on newborns therefore has been unavoidable. The knowledge gained by this research has been the basic condition for the introduction of a screening on the newborn hip by ultrasound leading to an earlier detection of malformations and by that to an earlier and more successful treatment. The dilemma as exemplified by the hip screening is world wide known, the convention tries to find a way out of this “No way out” (aporia), for which to find a solution satisfying everybody is difficult or even impossible.

The convention makes a difference between research with a potential direct benefit for the participant not capable to consent and without such an expected benefit.

From this basis different justifications for research on persons not able to consent are derivated.
In addition to the general provisions for medical research laid down in article 16 (see above) some specific conditions have to be fulfilled. The results of the research have the potential to produce a real, direct benefit for the health of the participant. There has been a long discussion on the wording “potential to produce”. Finally most of critical observers could be convinced, that research enters new fields having not yet specific indications for a certain benefit which has to be examined by the project. The word “potential” reflects this openness in an appropriate manner. Accepting the principle of potential direct benefit which may contribute to the best interest of the person not able to consent this kind of research is allowed in many states. The condition that research of comparable effectiveness cannot be performed on individuals capable to consent underlines the need to restrict research projects to fields where otherwise a better understanding or an improvement of treatment cannot be achieved. There has to be a legal representation in accordance with national law and the person concerned does not object. It may be sometimes difficult to assess an objection e.g. of a newborn or a very young minor.

For research on persons not able to consent the “potential direct benefit” for the participant may be accepted as justification for national law and for the authorisation to be sought of the legal representative.

Research without an expected benefit for the person concerned, necessary e.g. for the improvement of basic knowledge, needs some different considerations. For this type of research specific regulations have been introduced, discussed on wide a basis in Europe, accepted or refused (Fig 7)!

First of all it is stated that this kind of research should be an exception. Specific protective conditions have to be prescribed by law. A benefit for the participant is not excluded but in a serious calculation not expected. The research aims to produce results for the benefits of others as specified in the legal wording. Rather new at the time of the adoption of the Convention were the terms “minimal risk” and “minimal burden”. This is absolute limitations which must not be widened even in case when the research project seems to have a potential benefit for the participant. Also findings which could in an unexpected manner improve the basic knowledge must not serve as justification for altering these absolute limitations. “minimal risk” is dedicated to the objective risk of used methods as e.g. calculated on a statistic analysis. “minimal burden” covers the reaction of the participant to the intervention. Specific legal definitions of these principles, which have been introduced in a regulation for scientific research for the first time by the Convention of Oviedo, are laid down in the “Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research (2).

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<td>1 (not copied here!)</td>
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<td>2 Exceptionally and under the protective conditions prescribed by law, where the research has not the potential to produce results of direct benefit to the health of the person concerned, such research may be authorised subject to the conditions laid down in paragraph 1, sub-paragraphs i, iii, iv and v above, and to the following additional conditions:</td>
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the research has the aim of contributing, through significant improvement in the scientific understanding of the individual's condition, disease or disorder, to the ultimate attainment of results capable of conferring benefit to the person concerned or to other persons in the same age category or afflicted with the same disease or disorder or having the same condition;

ii the research entails only minimal risk and minimal burden for the individual concerned.

Depending on the year of adoption by the Committee of Ministers, the legal instruments of the Council of Europe have been signed and ratified by a rather great number of Member States (Fig 8). Adopting and ratifying international treaties by States is a long lasting procedure, but it will proceed.

**Work of the Council of Europe in the Field of Bioethics**

- **Convention of Oviedo (1997)**
  Entry into force: 1/12/1999; Signatures: 34; Ratifications: 21

- **Additional protocols**
    Entry into force: 1/3/2001; Signatures: 31; Ratifications: 16
  - Transplantation of Organs and Tissues (2002)
    Entry into force: 1/5/2006; Signatures: 20; Ratifications: 7
  - Biomedical Research (2005)
    Entry into force: 1/9/2007; Signatures: 21; Ratifications: 5
  - Genetic testing for Health Purposes
    Adopted by the CDBI: 8/6/2007

- **Recommendation on research on human biological materials (2006)**

**Fig 8.**

Independent of the legal status of these instruments in a state their contents influence in an enormous manner thinking and debates of the public, of the scientific community, of parliaments and even of courts.

The content is often considered as an internationally accepted opinion and advice for the application of biology and medicine in all specifications with regard to the protection of human rights. The instruments of the Council contribute to the aim of a European harmonisation in this field.

**References**

Additional Protocol to the Convention on Human Rights and Biomedicine concerning Biomedical Research, Council of Europe Treaty Series - No. 195
The work of the Council of Europe in the field of bioethics is composed by three elements: the Convention on Human Rights and Biomedicine, also known as Convention of Oviedo as a basis, the additional protocols for specific areas and recommendations.

Additional protocols as foreseen in article 31 of the Convention of Oviedo (1) are themselves legally binding instruments for the development of the principles of the convention in specific fields. The protocols shall be opened for signature only by signatories of the convention. A signatory may not ratify, accept or approve protocols without previously or simultaneously ratifying, accepting or approving the convention. This provision has the aim to prevent any kind of “shopping of protocol” without respecting the principles of the underlying convention. (For more details see the contribution of the author in this book “The Work of the Council of Europe in the Field of Bioethics.

Biomedical research is a specific field described above for the development of the principles of the convention. Biomedical research in its very wide range is increasingly performed, and the level of protection of human rights and fundamental freedoms for the participants should be harmonized at least within the Member States of the Council of Europe. Therefore it seemed justified to the CDBI\(^3\) to work on such an “Additional protocol concerning biomedical research” (2) as a basis for the internal legal regulations of these states.

An additional protocol has to respect the relevant provisions of the convention without necessarily repeating the exact wording. Such principles with regard to biomedical research are the protection of human rights and fundamental freedoms, the primacy of the human being, professional standards, free and informed consent, the protection of persons not able to consent, the protection of private life and the right to information or not information, the freedom of research subject to the provisions of the convention or other legal protections ensuring the protection of the human being, the approval of a research project by a competent body after review of its ethical acceptability and finally the prohibition of financial gain by the human body as such and the disposal of a removed part of the human body by the person concerned.

The protocol on biomedical research repeats in its first article the aims of the convention by addressing them to “any research involving interventions on human beings in the field of biomedicine”.

\(^3\) Steering Committee on Bioethics of the Council of Europe; Comité Directeur pour la Bioéthique
Scope

On this basis the scope of the protocol has been defined. It covers the full range of activities in the health field using interventions on human beings. The term “intervention” needs to be clarified. After long lasting debates the plenary agreed to a wording which reflects the broad range of interventions in research (Fig 1).

**Article 2 – Scope**

1. This Protocol covers the full range of research activities in the health field involving interventions on human beings.
2. This Protocol does not apply to research on embryos *in vitro*. It does apply to research on foetuses and embryos *in vivo*.
3. For the purposes of this Protocol, the term “intervention” includes:
   i. a physical intervention, and
   ii. any other intervention in so far as it involves a risk to the psychological health of the person concerned.

Fig. 1.

There has been no problem with the physical intervention like taking a blood sample. The question arose whether and to what extend research using questionnaires should be included. Those representatives of Member States which were against the application of the term to questionnaires argued that research using this instruments is very wide spread outside the field of medicine. Representatives in favour of that application underlined that depending on the content of a questionnaire it could be more harmful than a simple blood sampling. The adopted wording is a good compromise. It is intended to present a protocol for the protection of embryos, therefore the protocol does not apply to research on embryos *in vitro*. In contrast the protocol covers research on foetuses and embryos *in vivo*. Research on pregnant women or on their growing child for their benefit is not uncommon, an extension of the protocol seems therefore to be justified.

**General provisions**

Some general provisions taken from the convention have been already mentioned above. Specific provisions have been added. Research on human beings may only carried out if otherwise research of comparable effectiveness e.g. on animals, is not possible. The protocol emphasizes specifically the aspect of scientific quality in article 8. Research must be scientifically justified, meet generally accepted criteria of scientific quality and be carried out in accordance with professional obligations and standards. It has to be supervised by a researcher with appropriate experience in that research field. Supervisor may be
a specifically experienced physician as researcher or a researcher who is otherwise qualified for this task.

In any medical research the relation of risk and benefit merits a specific assessment. There is wide range between the ends “no benefit” and “potential direct benefit”. The general principle of the protocol (article 6) requires, that research shall not involve risks and burdens to the human being disproportionate to its potential benefits. On this basis the protocol foresees a stepwise assessment. For research without a potential direct benefit for the health of the participant, e.g. basic research on healthy volunteers, no more than acceptable risk and acceptable burden is allowed. Whether risk and burden in a given project comply with these conditions has to be proved by an ethics committee and in accordance with national law by a competent body before approval. In research projects with a potential direct benefit for the person concerned risk and benefit are assessed on the relation to the expected benefit. Specific conditions for risk-benefit assessment in research on persons not able to consent will be considered below.

**Ethics committee**

The important role of ethics committees for the protection of human rights and fundamental freedoms of research participants is recognised by several provisions in chapter III of the protocol.

**Article 9 - Independent examination by an ethics committee**

1. Every research project shall be submitted for independent examination of its ethical acceptability to an ethics committee. Such projects shall be submitted to independent examination in each State in which any research activity is to take place.

2. The purpose of the multidisciplinary examination of the ethical acceptability of the research project shall be to protect the dignity, rights, safety and well-being of research participants. The assessment of the ethical acceptability shall draw on an appropriate range of expertise and experience adequately reflecting professional and lay views.

3. The ethics committee shall produce an opinion containing reasons for its conclusion.

Article 9 states in its first paragraph (Fig 2) that research projects without any exception have to be submitted to an independent ethics committee for the examination of its ethical acceptability. For multinational studies such an examination has to be performed in each state with participants of the project. By this provision – a similar one exists in the EU Directive 2001/20/EC - the Council clearly refuses the well known suggestions coming from different groups that in multinational studies the assessment of only one ethics committees should be binding for all states.

The protection of the dignity, the rights, safety and well-being of the participant is in the focus of the ethical examination. It is often proposed or even asked by interested groups that ethics committees should restrict the examination
to these items without looking on other points like scientific quality. But the basis of the examination extended to the reflection of professional and lay views covers all relevant aspects.

Ethics committees expressed sometimes in the past only a favourable or a not favourable opinion concerning a submitted project without adding any reason for that outcome. The requested presentation of reasons for the conclusion found makes the process of decision more transparent specifically for the researcher as an applicant. An understandable and substantiated opinion is part of the improvement of medical research.

Ethics committees as competent bodies for the ethical examination should have a guaranteed independence. Parties to the protocol are asked to take measures to assure this independence and to prevent any kind of undue external influences (article 10). Members of the committee are obliged to declare all possible circumstances that might touch their independence. In a case of conflict of interests they should be excluded from the ethical review of the submitted project.

All necessary information for the assessment of a project shall be given to the ethics committee in a written form. In particular items contained in an appendix to the protocol (see appendix) shall be provided to the committee, so far as relevant for the research project submitted. This appendix has three chapters “Description of the project”, “Participants, consent and information” and “Other information”. The items in the appendix reflect the process of finding appropriate information during the period of preparation and adopting the protocol. The appendix may be criticized as being incomplete. However explicitly the ethics committee is given the right to request additional information if necessary for the examination of a specific project. The CDBI has preferred the form of an appendix for the items of information to be presented to the ethics committee. There may be a need in the future to change. An appendix can be amended much easier than a protocol and therefore be better adapted to new requirements.

A point of a wide spread discussion is the prevention of undue influence, which is not defined in the protocol, on persons invited to participate in a research project. The ethics committee must be satisfied that such an undue influence is not exerted including that of a financial nature. This obligation is usually fulfilled by asking the applicant of the examination to give a written specific declaration. The prevention of undue influence on vulnerable or dependent persons is an other obligation of an ethics committee (article 12).

**Information and consent**

Consent as necessary for any medical intervention is only valuable if it is based on an adequate and comprehensible information. In the research field the information has to cover the purpose, the overall plan and the possible risks and benefits. The information should include the opinion of the competent ethics committee as an independent view on the project and may help the participant or a legal representative in the process of decision making (article 13).

Information is considered as such an important issue that specific items are listed in the protocol (Fig 3). The participant should know details of the project.
and alternatives to it in prevention, diagnostic or treatment. He must be informed on the available measures in the case of adverse events and on the possibility of compensation. Compensation by insurance beyond drug research not prescribed in all states. The participant must be informed on the existence or non existence of compensation by insurance arrangements. During a research project results with relevance for the participant may be gained. The access to these data should be possible for the participant, at least be offered. The item of information on the overall results has been introduced to improve the openness of research. Why should an interested participant not know the results gained by his contribution? The knowledge of the source of funding may prevent a person to participate to a project paid by a sponsor to whose aims and intentions the person concerned is in conflict. The same prevention is covered by the information on any kind of further use as far it can be foreseen.

The regulations for the consent (article 14) follow the line drawn by the convention by repeating more or less its wording.

<table>
<thead>
<tr>
<th>Specific items for information (article13,2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• nature, extent and duration of the procedures involved; details of any burden imposed by the research project;</td>
</tr>
<tr>
<td>• availability of preventive, diagnostic and therapeutic procedures;</td>
</tr>
<tr>
<td>• response to adverse events or the concerns of research participants;</td>
</tr>
<tr>
<td>• respect for private life and ensure the confidentiality of personal data;</td>
</tr>
<tr>
<td>• access to information relevant to the participant arising from the research and to its overall results;</td>
</tr>
<tr>
<td>• compensation in the case of damage;</td>
</tr>
<tr>
<td>• source of funding of the research project</td>
</tr>
<tr>
<td>• foreseen potential further uses, including commercial uses, of the research results, data or biological materials;</td>
</tr>
</tbody>
</table>

Fig. 3.

Protection of persons not able to consent to research

The protocol follows the provisions of the convention by making a difference between research with a potential direct benefit for the participant not capable to consent and without such an expected benefit.

In addition to the general provisions for medical research some specific conditions of the convention are repeated. Generally the results of the research must have the potential to produce a real, direct benefit for the health of the participant. The condition that research of comparable effectiveness cannot be performed on individuals capable to consent underlines the need to restrict research projects to fields where otherwise a better understanding or an improvement of treatment cannot be achieved. Many states accept the principle of potential direct benefit as a contribution to the best interest of the person not able to consent. Consequently it gives the basis for the authorisation of research in this situation by legal representation acting in accordance with national law.
The legal representative or an authority or a person or a body as provided by law may authorise the participation in a specific, written form. Previously expressed wishes or objections of the represented person are taken into account. This wording is not binding in a legal sense, but will be in reality a strong provision for any thinking of authorisation against a previously expressed wish. However such an authorisation might be taken into account when at the time of research treatment options are available not yet in place in the moment of expressing a previous wish. An adult not able to consent shall as far as possible take part in the authorisation procedure. The opinion of minor shall be considered as an increasingly determining factor in “proportion to age and degree of maturity”. These specific provisions of article 15 should hinder any kind of authorisation against a detectable wish of a minor or of an adult. The article requires, that the person concerned does not object. It may be sometimes difficult to assess an objection.

Any authorisation must be based on adequate information given in a comprehensible form (article 16). Generally spoken, the requirements of this information are the same as those necessary for a person able to consent to research. Respecting the principle of participation of the represented person in the authorisation procedure the information shall be provided to that person if he or she is in a state to receive it.

Research without an expected benefit for the person concerned is covered by specific provisions. First of all it is stated that this kind of research should be an exception. Specific protective conditions have to be prescribed by national law. A benefit for the participant is not excluded but in a serious calculation not expected. The research aims to produce results for the benefits of others as specified in the legal wording. Rather new at the time of the adoption of the Convention were the terms “minimal risk” and “minimal burden”. This is absolute limitations which must not be widened even in case when the research project seems to have a potential benefit for the participant. Also findings which could in an unexpected manner improve the basic knowledge shall not serve as justification for altering these absolute limitations (Fig 4).

### Article 15, 2 - Protection of persons not able to consent to research

2. Exceptionally and under the protective conditions prescribed by law, where the research has not the potential to produce results of direct benefit to the health of the person concerned, such research may be authorised subject to the conditions laid down in paragraph 1, sub-paragraphs ii, iii, iv, and v above, and to the following additional conditions:

i. the research has the aim of contributing, through significant improvement in the scientific understanding of the individual's condition, disease or disorder, to the ultimate attainment of results capable of conferring benefit to the person concerned or to other persons in the same age category or afflicted with the same disease or disorder or having the same condition;
ii. the research entails only minimal risk and minimal burden for the individual concerned; and any consideration of additional potential benefits of the research shall not be used to justify an increased level of risk or burden.

Fig. 4.

The terms “minimal risk” and “minimal burden” as introduced by the Convention of Oviedo are defined for the purposes of the research protocol in its article 17 (Fig 5).

Article 17 – Research with minimal risk and minimal burden

1. For the purposes of this Protocol it is deemed that the research bears a minimal risk if, having regard to the nature and scale of the intervention, it is to be expected that it will result, at the most, in a very slight and temporary negative impact on the health of the person concerned.

2. It is deemed that it bears a minimal burden if it is to be expected that the discomfort will be, at the most, temporary and very slight for the person concerned. In assessing the burden for an individual, a person enjoying the special confidence of the person concerned shall assess the burden where appropriate.

Fig.5

“Minimal risk” is dedicated to the objective risk of used methods as e.g. calculated on a statistic analysis on the foreseen or not foreseen events using a specific method. Since this is a rather new approach scientific associations of researchers are invited to present examples which comply with “minimal risk”. At the time of the wording e.g. taking a little more of blood than needed for a necessary diagnostic procedure or removing a bit more tissue during a biopsy performed for diagnostic purposes have been discussed as interventions with minimal risk. There are examples in the explanatory report to the research protocol. “minimal burden” covers the reaction of the participant to the intervention. There may result very different reactions to interventions. Therefore it may be appropriate that a person enjoying the special confidence of the person concerned is asked to assess the burden. This person may be able to distinguish between a usual reaction to any medical intervention and to one which is due specifically to the intervention occurring as part of the research. To clarify the intention of this provision it is emphasized that for a diagnostic need the burden may be more than “minimal” whereas it is restricted to “minimal” without any exception in the case of pure research.

Specific situations

The provisions outlined for research on persons able to consent or not able to consent to research are in some manner adapted to specific situations:
research on pregnant women or persons deprived of liberty or in emergency clinical situations.

The general provisions for research apply if a direct benefit to the health of participants deprived of liberty or of pregnant women including foetuses or embryos is expected.

The provisions are specified in two situations – persons deprived of liberty or pregnant women - where a research project has not a potential direct benefit to the participants. These provisions are binding conditions and must not be overruled even not by consent to any other procedure given by the person concerned.

Research in pregnancy may be necessary for a better understanding of the pregnancy as such, or of the biological relation between mother and embryo or foetus as source of complications and of problems of the intrauterine development of the embryo or foetus. Results may contribute to a better medical care.

The protocol agrees to research on a pregnant woman without a potential direct benefit to her health or to that of her embryo, foetus or child after birth if additional conditions are met. These are derived comparably from those for research without a potential direct benefit on persons not able to consent. The research is undertaken with the aim to produce results contributing to the benefit to other women in relation to reproduction or to other embryos, foetuses or children. The already mentioned condition is underlined that research of comparable effectiveness cannot be performed on women who are pregnant. The research is limited to projects with “minimal risk” and “minimal burden”. When research is carried out on a breastfeeding woman, all necessary measures have to be taken to avoid any adverse impact of the child (article 18).

For research on persons deprived of liberty similar provisions are laid down in article 20. Research on this group entails the problem of the validity of a free and informed consent given under the conditions e.g. of a prison. Some states allow this kind of research on persons deprived of liberty, others do not. The protocol requires that there should be a legal regulation saying in the first words of article 20 “Where the law allows research on persons deprived of liberty…”.

There is without any doubt a need for research on persons in emergency clinical situations. As typical situations may be recalled stroke, myocardial infarction or traffic accidents. The physician has often only short time to start an appropriate treatment, the time span in general is not sufficient to seek any kind of authorisation if the persons concerned is not able to consent or is impaired to give a valuable consent. Until now there have been made only rare attempts to legal regulations. Thus in emergency situations a legal uncertainty is left to the physician whether to include or not a person into a research project.

The protocol presents by its article 19 an appropriate solution. Considering that human rights and fundamental freedoms may be touched, it is increasingly acknowledged that this field of research cannot be regulated by provisions of “soft law” like the Declaration of Helsinki or the guidelines of CIOMS.

Consequently the protocol requires that the performance of research in clinical emergency situations as such and the appropriate conditions shall be
determined by law. The article enumerates conditions for a legal regulation. The
person is not in a state to consent and because of the urgency of the situation it is
impossible to obtain in a sufficient time an authorisation from the legal
representation in accordance with national law. Research of comparable
effectiveness cannot be carried out in non-emergency situations. A specific
approval for research in emergency situation by the competent body is needed.
Any previously expressed objection shall be respected so far as known to the
researcher. This is the provisions for research with a potential direct benefit. The
protocol goes still a step forward by introducing the above presented provisions
for research on persons unable to consent without a potential direct benefit. For
this research the conditions “minimal risk” and “minimal burden” apply.
The protocol requires that the person concerned or the legal
representative shall be provided with all relevant information concerning the
participation as soon as possible. Than the person concerned may consent to the
continued participation or not or the legal representative may authorise it or not
(Fig 6).
This procedure of consent or authorisation may be classified as
“postponed or delayed consent”. It is totally different from any kind of waiver of
consent as proposed by some soft law.

<table>
<thead>
<tr>
<th>Research in emergency situations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protective conditions prescribed by law</td>
</tr>
<tr>
<td>Person not able to consent</td>
</tr>
<tr>
<td>Impossible to obtain authorisation from a legal representative</td>
</tr>
<tr>
<td>Research in emergency situation justified</td>
</tr>
<tr>
<td>Project approved specifically as emergency project by competent body</td>
</tr>
<tr>
<td>Research without potential direct benefit:</td>
</tr>
<tr>
<td>minimal risk and minimal burden</td>
</tr>
<tr>
<td>Information of person concerned or representative as</td>
</tr>
<tr>
<td>soon as possible - consent or authorisation for continued participation</td>
</tr>
</tbody>
</table>

Fig.6

**Safety and supervision**

Once a project has been approved measures for safety and supervision
during its performance need to be taken aiming the protection of participants
(articles 21–24; Fig 7).
Safety has to be ensured, risks and burden have to be minimised.
Minimal risk and minimal burden are not required by this wording, it only
means in this context to reduce risk and burden to a possible extent. Supervision
by a clinical professional with the necessary qualification and experience
contributes to the safety of the participants specifically in case of adverse events.
The health status of the person invited to participate has to be assessed
specifically in relation to the envisaged research project. A special attention shall
be paid to participants in the reproductive stage of their lives. Necessary clinical
interventions have priority and should not be withhold or delayed for scientific
reasons.
Safety and supervision

- Minimisation of risk and burden
- Non-interference with necessary clinical interventions
- Proven methods for control groups
- Use of placebo: no methods of proven effectiveness or withholding of such methods without unacceptable risk
- Re-examination of a research project in the light of scientific developments

Fig 7.

Research comparing different options of prevention, diagnosis or treatment needs control groups. There are several proposals concerning the appropriate methods of prevention, diagnosis or treatment to be given to the members of control groups. The main difference in all debates is focussed on the question whether it should be “the best method” or a “proven method”. The protocol states that the method for the members of a control group should be a proven one in the understanding proven as evaluated by accepted scientific methods. This wording does not at all ply for a lower standard for the control group.

The use of placebo in research may be necessary and justified under certain conditions. Following the protocol the use of placebo is permissible when methods of proven effectiveness are not yet developed or withholding or withdrawal of proven methods does not present an unacceptable risk or burden for the person concerned. The latter situation is known from studies on the treatment of pain and headache. The protocol does not accept any other justification for the use of placebo as e.g. scientific need as such as proposed by some soft law. After signature and ratification by a state any conflicts cannot be excluded by admitting other conditions for the use of placebo than codified by the protocol.

Research is an on going process, new developments arise nearly daily. Therefore the justification of any research project needs a re-examination in the light of those new developments. On the basis of this re-examination a decision is taken on the discontinuation or a necessary change of the project. The participants or the representatives need to be informed and, if appropriate in relation to the results of the re-examination asked for an additional consent or authorisation.

Sometimes research projects are terminated without any information of the reasons. Such information could e.g. contribute to prevent further research on the same field or using the same methods or when a failure has been demonstrated already by a project. To prevent such secret keeping article 24, 4 require that the competent body shall be informed of the reasons for a premature termination of a scientific project.

Confidentiality and right to information
The protection of privacy and the right to information are included in the convention giving the frame for appropriate provisions for the research field (Fig 8).

### Confidentiality and right to information

- Information of a personal nature: confidential
- Legal protection of confidentiality of projects submitted to an Ethics Committee
- Right of the participant to know any information collected
- Information of relevance to the health to be offered to the participant; information in the framework of counselling
- On completion: report or summary for Ethics Committee or competent body
- Appropriate measures to make public the results of the research in reasonable time

Any information of a personal nature collected during a research project is considered as confidential and therefore underlying the rules for the protection of private life. It should be noted that the protocol requires the protection of confidentiality and the prevention of any inappropriate disclosure of the documents submitted to an ethics committee by law. In accordance with article 10 of the convention research participants are entitled to know any information which has been collected on their health. During a research project information of relevance to the current or future health or quality of life of a participant may be gained. This information is offered to the person concerned, the participant may accept or refuse such information. If the person agrees the information is given within the framework of healthcare or counselling.

This provision shall exclude that a person is left alone with the information without any explication or comment. If appropriate necessary measures may be proposed to the person concerned also with regard to family members. The foreseen framework should guarantee the protection of confidentiality.

When the research project is completed a summary or a report should be submitted to the ethics committee or to the competent body. This provision aims to prevent any kind of disappearance of research results in the dark. Persons as participants of research may be interested to know the results of a project they contributed to. Therefore on their request the conclusions shall be made available.

A major issue of debates is the publication of results. Obviously favourable, so called positive results are published without delay. Such a publication is in the interest of the researcher and very often also of a sponsor e.g. a pharmaceutical company. On the other hand it is well known that in the case of not favourable, so called negative results, hesitations exist to publish. Publication may harm the reputation of the researcher or be in conflict with the aims and interests of the sponsor, not necessarily always a pharmaceutical company. Not favourable results have the potential of information on research
methods or steps which failed. By that information unnecessary repetitions of research projects with the inclusion of human beings could be avoided. Publication of not favourable results may be considered as a tool to learn, therefore those publications are part of an appropriate scientific conduct. It seems to be difficult or even impossible to legally force a researcher to publish. Therefore the protocol only obliges the researcher to “take appropriate measures to make public the results of research in reasonable time”.

It is at least assumed that biomedical research may be performed in states with different standards as compared to the protective provisions in other states. Article 29 “Research in States not parties to this Protocol” tries to safeguard that research in those states complies with the principles on which the protocol itself is based.

Finally the articles as part of the protocol so far as an instrument of the international right are mentioned but not considered in detail.

The additional protocol concerning biomedical research has got predominantly favourable reactions in the international debate on the regulations for the protection of human rights and fundamental freedoms of research participants. It does not hinder research in medicine for the ultimate attainment of better treatment.

It is predicted that this protocol will harmonise in the future the biomedical research at least within the Member States of the Council of Europe.

Appendix
“Appendix to the Additional Protocol on Biomedical Research
Information to be given to the ethics committee”

Information on the following items shall be provided to the ethics committee, in so far as it is relevant for the research project:

Description of the project
i. the name of the principal researcher, qualifications and experience of researchers and, where appropriate, the clinically responsible person, and funding arrangements;
ii. the aim and justification for the research based on the latest state of scientific knowledge;
iii. methods and procedures envisaged, including statistical and other analytical techniques;
iv. a comprehensive summary of the research project in lay language;
v. a statement of previous and concurrent submissions of the research project for assessment or approval and the outcome of those submissions;

Participants, consent and information
vi. justification for involving human beings in the research project;
vii. the criteria for inclusion or exclusion of the categories of persons for participation in the research project and how those persons are to be selected and recruited;

viii. reasons for the use or the absence of control groups;

ix. a description of the nature and degree of foreseeable risks that may be incurred through participating in research;

x. the nature, extent and duration of the interventions to be carried out on the research participants, and details of any burden imposed by the research project;

xi. arrangements to monitor, evaluate and react to contingencies that may have consequences for the present or future health of research participants;

xii. the timing and details of information for those persons who would participate in the research project and the means proposed for provision of this information;

xiii. documentation intended to be used to seek consent or, in the case of persons not able to consent, authorisation for participation in the research project;

xiv. arrangements to ensure respect for the private life of those persons who would participate in research and ensure the confidentiality of personal data;

xv. arrangements foreseen for information which may be generated and be relevant to the present or future health of those persons who would participate in research and their family members;

**Other information**

xvi. details of all payments and rewards to be made in the context of the research project;

xvii. details of all circumstances that might lead to conflicts of interest that may affect the independent judgement of the researchers;

xviii. details of any foreseen potential further uses, including commercial uses, of the research results, data or biological materials;

xix. details of all other ethical issues, as perceived by the researcher;

xx. details of any insurance or indemnity to cover damage arising in the context of the research project.

The ethics committee may request additional information necessary for evaluation of the research project.

**References**


Additional Protocol To The Convention on Human Rights and Biomedicine concerning Biomedical Research, (CETS No.195)
NATIONAL COMMITTEE FOR BIOETICS

UNESCO Commission of Serbia and Montenegro has founded on October 31, 2003 The National Committee for Bioethics of Serbia and Montenegro, with the aims to plan and organize activities concerning ethics in biomedical research. The National Committee for Bioethics was settled in Serbian Academy of Sciences and Arts.

Aims of the National Committee for Bioethics:
1. Promote ethical and legal aspects of research, their application, and spread of ideas and informations mainly through education.
2. Support action with the aims to increase understanding in the public, specialized and sensitive groups, and decisions of general and private character concerning bioethics.
3. Collaborate with international governmental and non-governmental organizations involved in the field of bioethics, as well as with national and regional committees for bioethics or similar bodies.

The Law on Health Care in Serbia (Sluzbeni glasnik RS, 107/2005)

The law on health care in Serbia (2005) provided regulation of research on human beings. The main objectives of the regulation are to establish a Central Ethics Committee of Serbia and local ethics committees (at the Clinical Centers and Hospitals).

ETHICAL COMMITTEE OF SERBIA (ECS)

ECS is a professional body, nominated by the Serbian Government. ECS proposes basic principles of professional ethics of health care workers, coordinate ethical committees from health care institutions in Serbia, monitors scientific research and clinical investigation of drugs and medical devices in health institutions from Serbia, decides and gives opinion about dispute questions, which are significant for scientific research, medical trials, as well as clinical investigation of drugs.

ETHICAL COMMITTEES IN HEALTH INSTITUTIONS

The main role of research ethical committees is to assess both the scientific and ethical aspects of submitted protocols. Ethical committees are responsible not only for approval of the protocol and its amendments but also for follow-up and monitoring of the trial after its closure. This last commitment is rarely fulfilled because of lack of time and resources assigned to the ethics.

An analysis of the work of ethical committee at the University Clinical Center in Nis (Serbia) reveals that major time was devoted to the: clinical investigation of drugs, treatment procedures (e.g. hemofiltration, automated
peritoneal dialysis, basal/bolus therapy by an insulin preparation), new diagnostic methods, etc.

**Patient as a Subject of Medical Trial**

Medical treatment, which have a nature of an experiment, can be performed only with full law capacity patient and his/her informed consent. Patient gives a written consent, after having been sufficiently informed about purpose, goal, procedures, expected results, possible risks, as well as about unpleasant side effects of experiment. Patient must be specialy warned about freedom to refuse experiment, to give up and cancel the consent.

**Clinical Investigation of Drugs**

Clinical investigation of drugs was requested by foreign pharmaceutical companies as a part of international collaborative studies or, more common, as a part of drug registration procedure in Serbia. The benefits of such studies are small for the patients involved, with drug supplied only in the trial period. With a relatively good health care system and inexpensive investigation, Serbia could attract major pharmaceutical companies to seek research collaboration.

**Informed Consent**

Informed consent is of great importance both in routine care and in clinical research. Even if information is given to the patient it is not always comprehended. In some studies in Serbia about one half of the patients had misunderstood the information.

Research involving children or persons unable to give consent, pregnant women or healthy volunteers for clinical trials is very sensitive, and major evaluation is to be done at the Central Ethical Committee of Serbia.

**Healthy Volunteers**

Clinical research involving healthy volunteers is important for advancing medical knowledge but raises a variety of ethical issues, many of which stem from the fact that such studies pose risks to research participants without the prospect of medical benefits to them.

Since regulation is not strict in Serbia, ethical issues in research with healthy volunteers should be reconsidered and the ethical requirements should include: scientific or social value; scientific validity; fair subject selection; favorable risk-to-benefit ratio; independent review; informed consent; respect for enrolled subjects.

**Persons Unable to Give Consent**

For persons unable to give a valid consent applicants should, in addition to the previous: indicate the degree of risk and burden involved for the subject; whether and how the persons might benefit from the procedures envisaged; indicate why it is necessary to involve persons unable to give a valid consent; describe what arrangements are made to seek the agreement of the person's parent, guardian or other representative.

According to EU regulation the applicant should: provide justification for such research in terms of the potential benefits of the research in relation to the possible risks to persons; indicate the number of persons involved and
describe the selection criteria; provide details of the arrangements made for providing information to persons and for obtaining informed consent; specify any payments, inducements or other benefits to be given to the persons concerned; describe the compensation and treatment available to subjects for trial-related injuries

**Research in Developing Countries**

When research is to be performed in developing countries and/or by partners from developing countries or when the results can be potentially applied in these countries, the applicants should also describe the arrangements for: sharing of benefits and allocation of intellectual property rights; contribution to capacity building in developing countries (i.e. capacity to assess and use modern technologies while respecting their own choices, needs and local conditions).

**Refugees and Internally Displaced Peoples**

A debate is now underway about the proper ethical guidelines to apply when doing research in refugee populations and among internally displaced peoples. The debate pivots on the tension between the need to develop evidence based emergency health measures and the need to protect vulnerable populations from possible exploitation or harm. A 750,000 population of these lived in Serbia.

**A Trial in Serbia Might be Justified in a Number of Ways**

The research might address an important health problem in the country. It might represent a joint effort by the country sponsoring or conducting the study and Serbia to address an important health problem in both countries. Conducting a trial in Serbia because it is more convenient or efficient or less troublesome to do so is never a sufficient justification.

When research is to be performed in Serbia, the applicants should also describe the arrangements for: sharing of benefits and allocation of intellectual property rights; contribution to capacity building in Serbia (i.e. capacity to assess and use modern technologies while respecting our own choices, needs and local conditions); the supply of new drugs must be guaranteed after a trial has ended, even for patients’ lifetime if necessary.

**Organ Donation**

A worldwide shortage of donor organs has led to the development of national and international systems for organ procurement and allocation. Such systems promote organ donation and ensure fair distribution of available donor organs. National system in Serbia is modestly developed. Organ trafficking and paid organs do not exist in Serbia.

**ETHICAL COMMITTEES OF MEDICAL FACULTIES**

According to the Statutes of the Medical faculties in Belgrade and Nis, their respective Assemblies for Education and Science, after the deans’
suggestion, appoint Ethical Committees, and through the appropriate decisions determine their composition, authority and mode of operation.

Ethical Committee according to the Statute of the Faculty of Medicine University of Nis (Article 55):

- Ethical Committee is formed to consider the ethical aspects of preclinical and clinical scientific research.
- Ethical Committee consists of nine members, with at least one external, non-faculty member and at least one who is not working in health care. One member of the ethical committee is a student appointed by the Student parliament.
- President, Deputy President and members are appointed by the Assembly for Education and Science after the suggestions of relevant departments and advisory board, for the period of 4 years.
- As required, Ethical Committee may engage a reknown expert.
- Work of the Ethical Committee is regulated by the Rules & Regulations brought forth by the Council of the Faculty of Medicine.
- Ethical Committee submits its reports to the Assembly for Education and Science of the Faculty of Medicine, at the end of each year, as a rule.
- Ethical Committee adopts its own ethical codex.

**Competence of the Committee (Article 4)**

- Creation of the rules, extent and content of ethical principles related to the activity of Faculty of Medicine UN
- Consideration of ethical principles related to research and education of teachers, associates and students of the Faculty of Medicine UN
- Analysis of ethics in practical work of teachers, associates and students of the Faculty of Medicine UN
- Monitor qualification and competence of researchers and analyzes possible risks in the phase of experimental work
- Provides human rights preservation in each investigation, especially human dignity
- Monitor research work related to children, pregnant women, mentally affected, prisoners and other vulnerable groups
- Defines principles of ethics of experimental work with animals.

**Research Ethics in Medical Curriculum**

There are lectures on clinical ethics in the medical curriculum, and it is also proposed that ethics committees play a central educational role by helping physicians to be aware of moral problems and by contributing to the training of research teams.

**ETHICAL COMMITTEE OF THE HEALTH CARE CHAMBER**

- Oversee ethical questions in medical, stomatological, pharmaceutical, biochemical, medical nurses and technician practice
- Give opinion on the practice of its members conform to the ethical codex
- Promote principles of the professional ethics in the view of attaining ethical standards in the activities of health professionals.

References


The practice of ethical committees in health institutions, as experts' bodies, which monitor the providing and practicing of health care on the base of professional ethic, especially in clinical trial of medicines, is wellknown in Serbia. Nevertheless, for many years there has been a little speach about duties related with this medical procedure, especialy about rights of a clinical trial subject. Very often legal aspects in pure medical discussion are not be presented. Practically, the situation was similar like in other countries from Balkan region. This was the consequence that generaly patients' rights were not sufficient developed nor protected in Serbia. The same was about pharmacy patients' rights. However, such a bad situation now is in the process of changing and Serbia have in this area some positive results. Legislation and regulatory frame can be explain by using two aspects: - law regulation (new health legislation in Serbia); - professional regulation in the domain of medical and pharmacist profession (new guidelines, ethical codes, etc). Significant part of reforming process is also reorganization and establishment of new ethical committees, particularly in local and the national level, e.g. Ethical Committee of the Republic of Serbia. The Health care Law in Serbia provides significant regulation of research on human beings and ethical committees are now composed to provide complete and adequate review of each research. It may be concluded that Serbian positive law in this area is mostly harmonized with several important European and international treaties.

Introduction

The aim of this review is to point out to the extent, how the current questions imposed by medical practice in Serbia are the subject of legal regulations, and especially in view of medical researches and work of ethical committees.

This review proceeds from a wider context first, as numerous issues have their basis in constitutionally guaranteed rights, criminal law sanctions and public law provisions. The Constitution of Serbia (2006) guarantees fundamental rights and health protection through its known principals:

- Human life is untouchable (Article 24)
- Human dignity is untouchable and everyone shall be obliged to respect and protect it (Article 23)
- Physical and mental integrity is inviolable (Article 25)
− Nobody may be subjected to torture, inhuman or degrading treatment or punishment, nor subjected to medical and other experiments without their free consent (Article 25)
− Protection of personal data shall be guaranteed (Article 42)
− All are equal facing the Constitution and law (Article 21)
− Attained level of human and minority rights may not be reduced (Article 20)
− Everyone have the right to protection of their mental and physical health. (Article 68)
− Health care for children, pregnant women, mothers on maternity leave, single parents with children under seven years of age and elderly persons shall be provided from public budget unless it is provided in some other manner in accordance with the law; Health insurance; health care and establishing of health care funds shall be regulated by the law (Article 68)
− Everyone has the freedom to decide whether they shall procreate or not. The Republic of Serbia shall encourage parents to decide to have children and assist them in this matter (Article 63)

The Constitution anticipates a new paragraph on the prohibition of human cloning within the Right to life provision (Article 24). This provision is thus given constitutional rank significance, although its place should rather be among criminal law subject matter. Nevertheless, this constitutional proclamation is understated, as the law further has to clarify the matter regarding therapeutically cloning.

Certain provisions of the Penal Code of Serbia (1977) should also be observed in view of rights in health. Chapter 14 anticipates criminal offences against human health, and especially:
− Unconscious cure of ill person (Article 126); A doctor who in providing medical services uses an evidently inadequate means or an evidently unsuitable treatment or fails to observe appropriate hygiene standards or evidently proceeds unconscientiously and thereby causes deterioration of a person’s health, shall be punished by imprisonment up to three years;
− Failure to Provide Medical Assistance (Article 127); A doctor who contrary to his duty refuses to render medical assistance to a person in need of such assistance, and whose life is in immediate and present danger shall be punished by imprisonment up to one year.
− Failure to Act Pursuant to Health Regulations during Epidemic (Article 123); Whoever during an epidemic of a dangerous contagious disease fails to act pursuant to regulations, decisions or orders setting forth measures for suppression or prevention thereof, shall be punished by fine or imprisonment up to one year.
− Grave Offences against Health (Article 135); if, due to the offence, a person sustains grievous bodily harm or serious health impairment, or death results to one or more persons, the offender shall be punished by imprisonment of one to ten years.
The Health Care Act of Serbia (2005) also considers the following as a criminal offence: A Health Institution will be fined with a penalty of 200,000 to 1,000,000 Dinars if:
- It does not insure the patient undergoing a medical experiment with a competent Insurance organization before beginning of experiment, or
- Medical experiment is carried out on the patient without previous consent of ethical committee of health institution,
- Uses new health technologies without consent of Ministry (Article 256).

HEALTH LEGISLATION

Health legislation in Serbia may be viewed in its development dimension through the past and present as the current valid (positive) right. Undoubtedly, it has a long tradition and good experience even from the period of the kingdom, and former Yugoslavia. However, the laws and regulations of the medical profession are mainly conceived in a traditional, paternalistic way when patients’ rights are in question. The modern concept of patients’ rights is a heritage of recent date. That concept is connected with the nineties of the last century, primarily with the Health Care Act (1992) which deals more closely with the citizens’ rights in health system. Further, with the proposal of the Charter on Patients’ Rights (1999) by the Nongovernmental organization (NGO) sector and the introduction of a Protector of patients’ rights by the decision of the Minister of Health (2002).

In recent times, considerable efforts have been put into reforming the health fields in Serbia, in view of understanding the basic concepts of medical rights, medical ethics in a new context, patients’ rights as well as safety and work effects of medical services. The activities of the legislator are becoming very important, as many matters are still not the subject of separate regulations. There are many situations where professional and ethic rules should be transcribed into rights, as only in that way their violation could be legally sanctioned. Apart from that, it is practically impossible to decide on any ethical matter without proceeding from the concept of medical rights and certain legal details for a concrete case, and visa versa. Special permeation of legal and ethical rules exists. All this is more obvious in the field of medical responsibility. The poor work in legislation up to now has also been present because collaboration between members of the medical and legal professions did not exist, so laws were exclusively written by doctors or pharmacists who were not skilled for that kind of work. In other words, there was no cooperation between health and legal policies which a government should lead, or recognizable goals which direction should be taken. The negative consequences are:
- "mechanical" approach to the patient’ rights (without right understanding)
- nonexistence of separately codification on patient’ rights
- Work of ethical committees is not yet guarantee for the respecting of patient’ rights, because of negative examples in medical practice
- it makes often artificial symmetry between physicians’ duties and patient’ duties, which are by Law essentially different notions

The present intensive work on legislature consolidated the conscience on the significance of human rights in the domain of health and the necessity for Serbia to join relevant international documents, especially to sign and ratify the Convention of Human Rights and Biomedicine (1997) and its additional protocols.

On the other hand, an everyday medical practice, especially in the area of particular medical procedures and medical research, often proceeds in a way that is not legally regulated nor standardized and thus not recognized. Doctors proceed from ethic rules without considering the legal framework enough. At times, they see legal regulations and certain obligations only on the patients’ side. Serbia still has problems in understanding, defining and protecting human rights in the domain of medicine, but in recent times, significant steps have been taken to change this situation:

First step - New Health Legislation

The Health Care Act (2005) includes, for the first time, some of the basic patients’ rights within a separate chapter and introduces the institution of a Protector of patients’ rights. The Act anticipates the most important rights: self-determination, autonomy, inform consent, privacy, and the right to complain. A special provision refers to the patient undergoing a medical experiment (Article 38):

Medical experiments may be carried out only on adult, competent patients and only with their consent. The patients consent must be written, after being well informed on the meaning, goal procedures, expected results, possible risks, as well as unpleasant accompanying circumstances of the experiment. The patient must be distinctly warned that he is free to refuse the experiment and that he may revoke his approval at any time. Exceptionally, a medical experiment may be carried out on minors and other incompetent patients, but only to their direct benefit and with written consent of their legal representative who was previously informed according to the law. The competent health worker conducting the medical experiment is obligated to take care that the life and health protection of the patient must always have an advantage over the interest of the state or science. The patient who suffers damage on his body or health has a right to compensation in conformity with the law, regardless of responsibility.

The health facility is obliged to insure the patient undergoing a medical experiment before commencement of the medical experiment in case of damage to the health of that person incurred by the medical experiment, in conformity with the law. A contract should also be concluded with the patient in whom the amount of necessary expenses, which inheres to the patient undergoing the medical experiment, will be determined. The patient shall have the right to participate in clinical testing of medicine and medical devices, in conformity
with the law that regulates the field of medicine and medical devices. The Ethical committee of the health institution, before commencement of a medical experiment, shall bring the decision on undertaking medical experiments on patients in that institution. It is prohibited to undertake experiments in private medical practice.

*Medicines and Medical Devices Act* (2004) regulates that clinical trial of medicinal product can be performed on human beings if it is justifiable from the point of health, but only with written informed consent, which is signed in the presence of one witness (Articles 49-61). As a new institution National Agency for Medicines and Medical Devices decides about request for authorization of clinical trial and documentation that is in conformity with the Good Clinical Practice in clinical trials (Article 53). Here should be noted that there is a certain unconformity between two law textes concerning the requested form of the patients’ consent.

*Ordinance on conditions and manner of clinical testing of medicines* (2007) prescribes special protection of minors as trial subjects (Article 17). According to this Ordinance settled requirements for informed consent are the highest. Namely, before the start of the clinical trials of the medicines trial subject signs declaration that he/she has been informed about the data and issues written consent in the presence of the witness (Article 12). The Ordinance has also provisions about detailed procedures and competent bodies (Articles 35-50), where the committee does not issue a positive decision the Agency will not issue authorization (Article 36). This Act provides as well control of Agency and supervision of National Committee (Article 40).

**Second step - Reorganization and Establishment of new ethical committees**

The advantages of establishing a national committee, health institution committees as well as their law regulation are being proven. Now, it is introducing by the Law an ethical committee (board) in every health institution (Article 143). The Committee represents an expert body that monitors the rendering and carrying out of health protection on the principles of professional ethics (Article 147). Its members are appointed by the Director of the health institution on proposal of the expert council.

Tasks of the *ethical committee of a health institution* (local):

1) monitor and analyze the application of professional ethics principals in performing health practice;
2) give consent for carrying out scientific researches, medical experiments and well as clinical testing of medicine and medical means in health institutions, namely monitor their execution;
3) bring decisions and consider the expert questions regarding taking parts of human body for medical and scientific-teaching purposes, in conformity with the law;
4) bring decisions and consider expert questions regarding application of measures for treatment of sterility by biomedical impregnation procedures, in conformity with the law;
5) monitor and analyze ethical relations between medical workers and patients, especially in the field of the patients’ consent for proposed medical measures;
6) monitor, analyze and give opinion on application of professional ethics principal in prevention, diagnosis, curing, rehabilitation, research, as well as introducing new health technologies;
7) contribute to creating a habit in honoring and applying professional ethics principals in health practice;
8) continuously give counseling on all matters in health protection;
9) consider other ethical matters of health institutions (Article 148).

Jurisdiction of the Ethical Committee of Serbia (national):
1) to propose the basic principals of professional ethics of health workers;
2) to monitor the application of professional ethics principals of health workers in performing health practice on the territory of the Republic;
3) to coordinate the work of ethical boards in health institutions;
4) to monitor the carrying out of scientific researches and clinical testing of medicine and medical means in health institutions on the territory of the Republic;
5) to decide and give opinions on controversial matters which are significant for carrying out scientific research, medical experiments as well as clinical testing of medicine and medical means in health institutions in the Republic;
6) to monitor the execution of decisions and consider the expert questions regarding taking parts of human body for medical and scientific-teaching purposes in health institutions on the territory of the Republic, in conformity with the law;
7) to monitor the execution of decisions and consider expert questions regarding application of measures for treatment of sterility by biomedical impregnation procedures in health institutions on the territory of the Republic, in conformity with the law;
8) to submit an annual report to the Ministry on the carrying out of scientific research and clinical research of medicine and medical means in health institutions on the territory of the Republic, as well as on the noted problems, flaws and complaints on the work of ethical boards in health institutions;
9) to consider other matters of professional ethics in carrying out health protection (Article 157).

**National Agency for Medicine and Medical Devices** is obliged to inform the Ethical Committee of Serbia on the carrying out of clinical testing of medicine and medical means for which a permit was given, in conformity with the law that deals with medicine and medical means. The Agency for Medicine and Medical Devices of Serbia may, before giving the permit, request the opinion of the Ethical Board of Serbia on the submitted request, namely on all controversial matters which may arise during clinical testing.

A Health Council of Serbia has been formed on the republic level, as an expert and counseling body that cares for the development and quality of the health protection system, the organization of health services and the system of
health insurance (Article 150). The work of the Health Council is public and its jurisdiction is as follows:

1) to monitor the development of the health protection and health insurance systems in the Republic and their coordination with European and international standards;
2) to propose measures for preserving and promoting state of health and strengthening the population health potential;
3) to propose measures for uniform realization of health protection of all citizens in the Republic, as well as measures for promoting health protection of populations at risk;
4) to propose measures for the functioning of the health system based on principals of continuance and efficiency;
5) propose measures for the functioning of compulsory health insurance on the principals of continuance, economy and efficiency, as well as measures for establishing and development of other forms of health insurance;
6) to evaluate the program quality of continual education of health workers and health associates (hereinafter: accreditation of the program of continual education);
7) to give opinions on health personnel development plan proposals;
8) to give opinions on enrollment into faculties and health schools policies and to cooperate with competent state bodies and other expert bodies in proposing measures of more rational enrollment policies into faculties and health schools;
9) to give initiative and propose measures with an aim to carry out reforms in the field of health protection and health insurance;
10) to consider other matters in the field of health protection and health insurance and offer expert assistance to governmental agencies, organizations and institutions in the realization of tasks which refer to social health care;
11) to carry out other tasks, in conformity with the law (Article 154).

Analyzing the jurisdiction of different committees defined by the Serbian laws it can be concluded that the competencies of local and national committees are not sufficiently clear divided. The national committee according to the valuable solution presents exclusively second instance body, and nothing else. In the same time, local committees have also duties to monitor and control clinical trial in their institutions. Regarding this situation it can not be seen clearly what had been the real intention of the legislator.

Third step -Other regulations

Serbia has adopted new codes of professional ethics in medicine (2007) and pharmacy (2001), as well as guidelines for good medical practice of primary health care. However, there are still deficits in guidelines for other medical fields. A new Code of Practice on clinical testing of medicine was in preparing. There is an ever-increasing transparency, openness and intra-disciplinary approach to solving current matters in the field of medicine.
**Conclusion**

The current state of health legislation in Serbia is largely coordinated with the leading solutions in Comparative law and with corresponding European and international treaties covering the area of human health. This especially applies to the field of pharmaceutical law and clinical testing of medicine in Serbia. In other fields though, there is still work to be done in bringing and revising several special laws, such as on artificial insemination, genetic testing, transplantation, blood transfusion, mentally ill persons, and there are proposals for adopting a special law on patients’ rights. Apart from that, it is necessary for Serbia to approach international and European documents in this field, as it will considerably improve reformation of Serbian Law in the sense of filling in the existing legal gaps (*lacuna iuris*) and active participation in the harmonizing process.

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UNESCO PROJECT OF PUBLIC AND PHYSICIAN AWARENESS OF GENETIC TESTING IN SERBIA

Zvonko Magić1, Sinisa Radulović2, Mirjna Branković-Magić2, Radmila Janković2, Dragoslav Marinković1, Snezana Pajović1, Silvio Dottorini3

1National Committee of Bioethics of Serbia, Belgrade, Serbia
2Institute for Oncology and Radiology of Serbia, Belgrade, Serbia
3UNESCO ROSTE, Venice, Italy

Introduction

During 2005 Pilot program Public and physician awareness of genetic testing in ethnically diverse populations (PPAGET project), created and financially supported from UNESCO Regional Bureau for Science in Europe was carried out in Serbia & Montenegro, FYR Macedonia and Slovakia. Investigation was addressed to estimate general practitioners knowledge concerning availability and use of genetic testing and counseling. Also, investigation was performed among lay public as potential user of gene tests aimed to estimate general population willing to participate in the process of genetic testing.

Similar investigations were not performed in our country and data collected in this program are of a great value in planning further activities concerning innovative education about progress in medical genetics directed to general practitioners, as well as popularization of genetic testing for early detection of hereditary diseases in general population.

Material and Methods

Current status of public and general practitioners awareness of genetic testing was reached throughout the use of two separate questionnaires, created with participation of investigators from Serbia, Greece, Slovakia, FYR Macedonia, and Italy. Applied procedure of data collection was realized in agreement with UNESCO-ROSTE, National Committee for Bioethics of Serbia and Montenegro, as well as Ministries of Health of Serbia and Montenegro.

According to the population size of Serbia & Montenegro, the estimation is that sufficient size (minimal number of participants) would be 600 lay persons. Estimation of drop out is 15% indicating that about 700 questionnaires must be delivered. Sufficient sample size for general practitioners, calculated according to total number of physicians in Serbia & Montenegro, together with 15% drop, was 300 physicians from primary health care services.

Survey for lay public was carried out through the use of common questionnaire with 19 questions. The questionnaire was structured in such way that questions with personal data (gender, age, education level etc), data about general knowledge on genetic testing (for example: do you know if genetic tests
can determine a defect in the fetus before birth), personal willing to participate in genetic testing if it is necessary, as well as with availability of genetic testing in our country, were grouped. The answers were offered through yes/no or multiple choice and had to be marked.

The interview of lay public was done during three consecutive weekends in April and May 2005 at the corridors of the biggest shopping centers in Belgrade. Besides Belgrade, lay public survey was performed in 1 center from Vojvodina, from Central Serbia and 1 from Montenegro. The activities were completed in two months (April and May 2005).

Survey for general practitioners was carried out throughout questionnarie with 21 questions to estimate the level of knowledge and rational use of available genetic tests within medical community. Similar to questionnarie for lay public, this one was also composed of the groups of questions with personal data, data describig level of knowledge about genetic diseases, as well as awareness of availability of genetic testing in our country.

Data from physicians working in primary health care were gathered at the Conferences for GPs that were organized in 6 centers in the different parts of Serbia & Montenegro (Health Center Vozdovac in Belgrade, Kladovo, Jagodina and Gornji Milanovac in Central Serbia, Subotica in Vojvodina and Podgorica in Montenegro). The questionnaires were delivered on the beginning of each conference and the participants have been asked to completed them. After that, the participants were informed about current status of clinical genetic testing through four lectures concerning possibilities for genetic testing in Serbia & Montenegro, laboratory gene tests, and current status of hereditary cancer syndromes management. Besides that, questionnaires were distributed to directors of additional Health Centers (6 from Central Serbia, 5 from Vojvodina) ensuring reliable data about physician's awareness of genetic testing.

**Data gathered in two ways**

1. Mailing of Questionnaires (10 centers)
2. Conferences for GPs (6 centers)

The questionnaires were delivered on the beginning of each conference.

**Lectures on**

1. genetic tests/methods
2. Hereditary cancer syndromes management
3. BRCA testing
4. Treatment options

**Results**
Results of surveys comprise creation of two data bases – first for GPs (283 questionnaires) and the second for lay public (865 questionnaires). Some of the persons included in survey did not complete whole questionnaires i.e. did not answer one or more questions. Questionnaires with lack no more than one answer were also included in survey Since the results have been expressed as percent (%), percent of opposite answers does not reach 100%.

**Lay public survey:** More than 2/3 of invited persons consented orally to take part of the survey and 865 questionnaires were collected. Among the persons who completed data, 530 (61%) were women and 334 (39%) men. Median age was 37±12 (SD) years with youngest participants being 18 and the oldest 65. More then half (57%) were very well educated and living in the cities (85%) and were employed (75%). Two-thirds were heard about genetic testing (Figure 1), but half of them do not know that tests are available in Serbia health system (Figure 2).

![Figure 1. Information about the term of genetic testing](image1)

![Figure 2. Information about the availability of genetic tests among lay public](image2)

Most (three out of four) of the participants believe that genetic tests are helpful (Figure 3).

Also, majority of the participants (94%) would agree to have genetic testing if certain disease is repeated in their families. 86% of the lay public is ready to participate in the genetic testing. Only 14% are not willing to participate. 90% of the participant is willing to share genetic test results with other members of their family (Figure 4).
The obtained results showed that majority of persons included in survey knew that inherited diseases could be transmitted to off-spring from both parents (Figure 5).
p<0.001
• Number 1: Belgrade (n=79)
• Number 2: city inside of Serbia (n=46)
• Number 3: countryside (n=39),

Figure 6. Results of lay public knowledge about genetic tests.

Figure 7. Comparison of results of lay public knowledge about genetic tests between Serbia and FYROM.

General practitioners survey: “Response rate” to the questionnaire was 100% for the questionnaires sent by regular mail. Conferences were very well
accepted by the colleagues. Total number of 283 physicians working in primary health care were surveyed, 76.6% women and 32.4% men. Median age was 44±9 (SD) years with youngest participants being 25 and the oldest 65. Among the participants, 65.6% of them had a specialization, whereas 34.4% did not have one. Time period from obtaining a medical diploma was in average 18 years (range 1-39 years).

More than half (57.5%) of the participants were not aware of medical and scientific progress on medical genetics. National medical journals and internet were quoted as the most frequent sources of news in medical genetics (Figure 8.)

![Figure 8. Awareness of medical and scientific progress on medical genetics](image)

Half of the participants (52.4%) considered that their level of knowledge of medical genetics has not been satisfactory for the requirements of their clinical practice (Figure 9.)

![Figure 9. Satisfaction with the knowledge of medical genetics](image)

![Figure 10. Awareness of the possibilities for further learning of new trends in medical genetics in Serbia & Montenegro](image)
More than half of the participants (67%) are thinking that there aren’t adequate possibilities for further learning of new trends in medical genetics (Figure 10).

Almost 90% of the participants gave correct answer on the question whether genetic testing can be used in the detection, prognosis and therapeutic decisions on some non-inherited diseases. Further, majority of the participants (85%) suggested that genetic counseling to an individual should be provided through the specialized genetic service and almost all of the participants believe that development of criteria or protocols for ordering genetic tests will be useful in primary and secondary health care (Figure 11).

![Figure 11. Usefulness of the new protocol for ordering genetic tests in primary secondary health care](image1)

![Figure 12. What is the medical justification for genetic testing of adult individuals?](image2)

It is important to point out that almost all of the participants gave correct answer that the personal or family history of a known or suspected genetic disorder is the main medical reason for prenatal genetic testing (Figure 12).

About 66% of general practitioners know where to refer the patient with hereditary predisposition (Figure 13). Half of the participants (52%) are thinking that genetic testing is not covered by health insurance in our country and surprisingly, also about half (54%) of the participants are not able to guarantee to the patients that the results of their genetic tests will not be divulged to third parties.

![Figure 13. Question to the participants where to refer](image3)
their patient for a hereditary predisposition testing

Figure 14. Comparison of results of general practitioners knowledge about genetic tests between Serbia and FYROM
Discussion and conclusions

The results of surveys in Serbia will be further compared with the results obtained with the same authorized questionnaires in Slovakia and Macedonia. Concerning the results of survey for lay public major findings are:

- Two/thirds of the participants in the lay public group were informed about the term “genetic testing”.
- But, half of them did not know whether genetic tests are available for them.
- Majority thought that tests are helpful, especially for the detection of defects in the fetus before birth, and expressed willingness to be tested.
- However, more than two/thirds do not know if genetic testing is covered by their health care insurance.
- Belgrade public is better informed about genetic testing than public from the sites inside of Serbia or villages concerning 2 from 3 questions that requires knowledge – if genetic tests can determine a defect in fetus before birth and if healthy parents can have a child with inherited disease.
- Educational level in Belgrade is similar to those in sites in sites inside of Serbia. In Belgrade and smaller cites educational level is better than in villages.
- Consequently, obtained differences in knowledge about genetic testing are not completely influenced by differences in educational level.
- Half of Serbian participants do not know that genetic tests are available in health system vs. 34% in FYROM.
- More than one third of participants from Serbia are not aware that genetic test might be performed by using blood sample vs. 16% in FYROM.
- More than 2/3 of participants in both countries believe that genetic test may determine defect in the fetus before birth.

General practitioners survey indicates the following:

- GPs express their thought that they are lacking of adequate knowledge concerning medical and scientific progress on medical genetic. They are not satisfied with the information they are receiving about latest development in genetic testing. In addition, they believe that there are no adequate possibilities for further learning on this topic.
- They believe that the development of protocols (guidelines) for genetic testing might be very useful.
- One-thirds of the GPs did not know where to refer the patient for hereditary predisposition testing.
Half of the physicians do not know if the genetic testing is covered by health care insurance.

Almost half did not give correct answers on specific questions about how autosomal recessive diseases are inherited or whether Down syndrome is inborn or inherited disease.

With increasing of time interval after graduation significantly decreases GP knowledge about medical genetics.

Physicians in the primary health care system are lacking basic knowledge about the medical genetics. There is no organized system for their information on such topic.

They are willing to refer their patients but there is no adequate information about protocols, referral system, insurance etc.

57% of Serbia GPs know that Down Syndrome is an inborn disease vs. 46% of GPs from FYROM.

More than half of the participants (58%) from Serbia answered that inherited diseases have been passed on in the next generations through both parents vs. 42% from FYROM.

Even more than 50% of GPs from Serbia are not able to guarantee confidentiality of genetic test results to their patients on the contrary to 20% of GPs from FYROM.

In order to improve the knowledge about genetic testing, it is necessary for our health care system to organize more efficient information system both for the lay public and for the physicians working in primary health care.

In conclusion, in order to improve the knowledge about genetic testing, it is necessary to perform more aggressive campaign for lay public throughout media and to create special educational programs for individuals and families at risk for hereditary disease. Also, innovative education about progress in medical genetics, throughout Continual Medical Education at Medical Schools, as well as throughout professional societies and Ministries of Health (Serbia) is required for physicians. Creation of guidelines for hereditary diseases for which predisposition can be tested would be of great value.

References


Metamorphosis of (bio) medical ethics

1. Hippocratic ethics
   (from Old Age till cca 50-60ies of XXth century)
2. philosophical (ethical) analysis of the issues in medicine, health care, biology, (bio)technologies, genetics, public health, etc.
   – birth of bioethics, principlism, ‘school bioethics’, ethics committees, bioethics centres (60-70ies of 20th century)


Last decades of 20th century ► New ethical problems in biomedicine

• biomedical research, clinical trials of drugs, informed consent, clinical trials in developing countries, placebo in research, justice and freedom of research, scientific honesty vs. dishonesty, good scientific practice,…
• gene manipulation, gene therapy, human enhancement, new ‘eugenics’
• stem cells, “therapeutic cloning”, somatic stem cell research,…
• assisted reproduction, in vitro fertilization, surrogate motherhood, gamete donation, cloning, biobanks, chimeras,…
• prenatal diagnostics, pre-implantation diagnostics, human embryo research, ‘supernumerary embryos’(?), embryo adoption,…
• fertility regulation, contraception, abortion, post-abortion syndrome,…
• euthanasia, terminal care, elderly, terminally ill patients, palliative care, death, brain death, assisted suicide, thanatology,…
• mental health, mental disorders/diseases, disorders of mental development, psychopathies, neuroses, drug therapy, neuroethics, …
• disorders of human psycho-sexual development, homosexuality, psycho-sexual immaturity, transsexualism,…
• transplantation of organs and tissues (living/dead donor,…),…
• xenotransplantation, transgenic animals,… (etc, etc.)
Bioethics for 21st century: Many Questions

- Commissioning ethics? Institutionalization of ethics?
- Bureaucratization of ethics? Only ‘procedural ethics’?
- Replacing ethics by sci/tech excellence?
- Mere legalism? Pure philosophy? Politics?
- Ethics by experts? Buying ethics/ethicists?
- Secular only? Place of religion/s? Cultures?
- Individual: Freedom vs. Responsibility?
- Personal moral integrity? Conscientious objection?
- Ethics in the public square? Dialogue vs. struggle?
- Consensus vs. compromise vs. democracy?
- Ethics by voting? Ethics by reasoning?

Various Types of Bioethics Institutions

- **ethics committees**, councils:
  - governmental (NECs,....)
  - non-governmental
  - international (e.g. IBC,....)
- bioethics associations
  - national
  - international
- institutes, centres, university departments,....
- periodicals (journals, newsletters,....)
- databases, information centres
- bioethics consultation services (e.g. clinical ethics)
- [“bioethicists”]

Bioethics and International Institutions (1)

- **European Union →** European Commission, Brussels
  - European Group on Ethics (**EGE**)
  - **NECs Forum**
  - Directorate „Science & Society“ (DG Research)
  - groups of experts (e.g. research ethics review panels)
  - research projects in/on bio/ethics (e.g. EURETHNET, EUREC,....)

- **Council of Europe**, Strasbourg
– Steering Committee on Bioethics (*CDBI*)
– *COMETH*

- **World Medical Association** (WMA), Genéve
- **World Health Organization** (WHO), Genéve (working/experts’ groups)
- **CIOMS**, Genéve
- **UNESCO**, Paris, New York
  - Intergovernmental Committee on Bioethics (IGCB)
  - International Committee on Bioethics (IBC)

**Bioethics and International Institutions** (2)

- International Association of Bioethics (IAB)
- European Association of Centres of Medical Ethics (EACME)
- Central and East European Association of Bioethics (CEEAB)
- European Forum for Good Clinical Practice (EF GCP)

- **USA**
  - President’s Commission (on Ethical Aspects of Biomedicine)
  - Institutional Review Boards (IRBs)
  - Office for Human Subjects Protection
  - centres, institutes, chairs of bioethics, medical ethics
    - The *Hastings Center*, Garrison, NY
    - *Kennedy Institute of Ethics*, GU, Washington, DC
    - Center for Health Care Ethics, SLU, St. Louis, MI
    - etc., etc.

**Council of Europe**

- Steering Committee on Bioethics  [*CDBI*]
- European Conference of National Ethics Committees  [*COMETH*]

**Council of Europe (CoE)**

Steering Committee on Bioethics (CDBI)
• **History:**
  – 1985: Ad hoc Committee of Experts on Bioethics (CAHBI)
  – 1992: Steering Committee on Bioethics (CDBI)

• **CDBI:**
  – steering committee
  – responsible for the intergovernmental activities of CoE in the field of bioethics
  – its work has led to the adoption of *Recommendations* of the Committee of Ministers and to the preparation of the *Convention of Human Rights and Biomedicine* (Oviedo, 1997) and *Additional Protocols* to the Convention
  [www.coe.int/T/E/Legal_Affairs/Legal_co-operation/Bioethics/CDBI]

**CDBI: ‘Oviedo Convention’ & Additional Protocols**

• *Convention of Human Rights and Biomedicine* (Oviedo, 1997)
• *Additional Protocols*
  – Protocol on genetic testing for health purposes (2007)
  – PENDING: Protocol on genetic tests – workplace, insurance, Protocol on the protection of human embryo and foetus, Guidelines for ECs
  [www.coe.int/T/E/Legal_Affairs/Legal_co-operation/Bioethics/CDBI]

**CDBI: Recommendations - Committee of Ministers of CoE**

• *Recommendations* (2001 – 2006)*
  – 2001 Recommendation Rec (2001) 5 on the management of organ transplant waiting lists and waiting times
  – 2002 Recommendation Rec (2002) 9 on the protection of personal data collected and processed for insurance purposes
  2003 Recommendation Rec (2003) 12 on organ donor registers
  2003 Recommendation Rec (2003) 24 on the organisation of palliative care
  2004 Recommendation Rec (2004) 8 on autologous cord blood banks
European Conference of National Ethics Committees – COMETH

The conference is composed of representatives of National Ethics Committees (or equivalent bodies) set up in Member States of the Council of Europe.

COMETH - FUNCTIONS

The purpose of the conference is to:

• promote co-operation btw. national ethics committees, notably by encouraging exchanges of information, sharing of experience; developing a European database; carrying out studies on questions of common interest; organising meetings at European or regional level;
• help countries wishing to set up a national ethics committee to set one up and run it
• promote, on a pluralist basis, public debate on ethical issues raised by progress in the fields of biology, medicine and public health

COMETH – ACTIVITIES

• activities of COMETH aimed to make an appropriate contribution to the public debate provided for in Article 28 of the Council of Europe Convention on Human Rights and Biomedicine,
• specific nature and independence of COMETH, which is responsible, inter alia, for discussing current ethical issues,
• complementarity between the activities of COMETH and the work of the Steering Committee on Bioethics (CDBI), (Resolution No. 1 of COMETH, Article 5)

COMETH Conferences

• 1st meeting, Madrid (1992); COMETH set up;
• 2nd meeting, Stockholm (1994);
• 4th Conference, Oporto (1998), “Controversial Ethical Issues in the Field of International Biomedical Research”;
• 6th Conference, Paphos (2001), “Genetics and Society: Opportunities and Threats”;
• 7th Conference, Strasbourg (CoE, 2003), “New Ethical Challenges - Bioethics Education and Biobanks”;
• 8th Conference, Dubrovnik (2005) “Meeting the Challenges of Changing Societies”

European Union

• European Group on Ethics in Science and New Technologies [ E G E ]
• Forum of National Ethics Councils [ NECs Forum ]
• Directorate „Science & Society“ (within DG Research)
• groups of experts (e.g. research ethics review panels)
• research projects in/on bio/ethics (e.g. EURETHNET, EUREC, EHBPO, EUROSTEM, …)

European Group on Ethics [ E G E ] in Science and New Technologies

• History:
  – 1991-1997: Group of Advisers on Ethical Implications of Biotechnology (GAEIB)
  – 1997-2000: EGE (1st mandate): 12 members
  – 2001-2005: EGE (2nd mandate): 12 members

• EGE:
  – an independent and multidisciplinary consultative body to the European Commission, composed of 15 members
  – in the EGE membership, necessary to ensure an appropriate range of professional skills and experience
  – members are appointed ad personam for their personal competencies and qualities

National Ethics Committees (NECs)

National advisory bodies on questions of ethics in science, research, ncl. biomedicine, and health care.

National Ethics Committees (NECs)

- issues relating to biomedical ethics are now especially important for society,
- NECs, in the states where they exist, have acquired substantial authority since they were set up,
- different States are planning to set up NECs or similar bodies,
- marking diversity of NECs (set up, composition, tasks, responsibility, legal backing, procedures, etc.)
- co-operation and pooling of experience between different NECs in Europe necessary

(Resolution No. 1 of COMETH, Article 5, 1999)

NEC - their place in the (health care) system

Parliament

Government

Ministry/ies

NEC

Professionals

Media

General Public

NEC and Ethics in Research and Science – Tasks

- national advisory body for ethics in R & S
- review, recommendations, initiatives concerning national laws, regulations, guidelines, etc.
- consultation role for local RECs
- opinions on particular ethical issues in R & S
- education of professionals & general public
- public debate
- international networking, exchange, collaboration, harmonization (?),
- exceptionally - review of research protocols
  (or specialized (R)EC with nation-wide competence)

**NECs - Present Situation**
- Council’s of Europe Comparative Study - 1998 (Sabatier, S., 2000)
- ECs in Central and Eastern Europen Countries (Glasa, J. (Ed.), CE & IMEB Fdn., 2000)
- Fuchs, M.: NECs, NEC of Germany, 2005
- EF GCP – Ethics review of CTs Protocols in EU countries, 2007  
  [www.efgcp.be]
- EGE Secretariat – newsletter: Ethically Speaking
- other surveys, occasional reports, etc. (?)

**NECs - CE Comparative Study (1998)**
- established on permanent basis by: law (7), decree (4), ministerial decision (3), government regulation (1), co-operation agreement (1), other (2)
  *German ECs’ Union, **National EC, *** C. on Biomedical Ethics
  (Sabatier, S., 2000)

**NECs - CE Comparative Study (1998)**
- most are independent, government supervision (3)
- financial management:
  - NEC’s own budget (6)
  - funded by the government (1)
  - funded by the Ministry of Health (4)
  - funded by a medical body (6)
  - funded by a private body (1)
- no renumeration for members, allowances (3)
- membership: 11 - 78 persons (average cca 15)
- members - experts in their field (lay persons ?!)
- multidisciplinary
  ( Sabatier, S., 2000)
NECs - CE Comparative Study (1998)
• referral of cases:
  – mostly submitted by the official authority
    (government, ministers, parliament, MPs, president)
  – submitted by less official authority
    (university, medical association, institution, NGOs, etc.)
  – initiative of the NEC itself
• mostly working using subcommittees, technical teams, working groups,
  outside experts
• decisions by:
  – consensus (8)
  – consensus, voting possible (4)
  – rarely by vote (3)
  – vote (3)
  (Sabatier, S., 2000)

NECs - CoE Comparative Study (1998)
• dissenting opinions:
  – mostly mentioned in the opinion
  – merely expressed
• opinions prepared for the government, ministry, parliament, public,
  health professionals
• mostly some impact on legislation
  (in some no legislation impact at all)
• public, media:
  – mostly NEC’s meetings are closed for the public
    (only a few allow public)
  – some NECs organize events aimed at public
• “...seems that public holds NECs in very high regard, but knows relatively little about them...”
  (Sabatier, S., 2000)

Main challenges for NECs in the next 10 years (1)
• Status of the embryo and experimentation in this field, use of genetics,
  medicine and financial issues.
• Acceptance of the contemporary bioethics.
• Importance of science in the society.
• International nature of research, harmonization, evolution of the basic ethics criteria.
• Application of ethics to changes in medical practice.
• Co-operation with other NECs in Europe, improvement of the NECs’ work.
• To show to the public and the biomedical community the importance of the ethical decision-making.

(Sabatier, S., 2000)

Main challenges for NECs in the next 10 years (2)
• Erosion of the use of norms and difficulty to obtain a consensus, adaptation and anticipation of the progress in science.
• Introduction of the relevant legislation, higher profile, increasing the awareness of ethical issues.
• Functioning of the review system in accordance with the law.
• Legislation concerning bioethics (namely the issue of medically assisted procreation), education, adoption of the Convention on Bioethics.
• Ethical issues raised by genetics.
• Improvement of the rights and dignity of the patients.

(Sabatier, S., 2000)

Main challenges for NECs in the next 10 years (3)
• Recognition and respect of the population, of the medical society and of authorities.
• Ethical and legal positions concerning some specific issues in bioethics (human embryo, human genome, terminal care, etc.), education.
• Allocation of health care resources, euthanasia, status and activities of non-conventional medical practitioners.
• Invasion of lawyers into the numerous fields of health care (legalism).
• Requests will be put to use.

(Sabatier, S., 2000)

Ethics Committees for Research Initiatives for Improvement
• Council of Europe - Program DEBRA
  (international conferences, workshops, documents, legal expertise, networking,…)
• Council of Europe – activities of CDBI, COMETH
• European Commission – Directorate General for Research, Science and Society Section:
  – European conference of research ethics committees, Brussels (January 2005), project EUREC
  – European Observatory on ethics in science and research
  – reports on legal situation in science and biomedical research (incl. ECs)
• **European Forum for Good Clinical Practice**  (international conferences; production of guidelines, other publications; educational activities; networking,…)

• **WHO**  (international conferences; production of guidelines, other publications, educational activities, networking,…)

• **CIOMS**  (international conferences; guidelines, …)

• **DIA, IPQC**; other professional or postgraduate /continuous education & training organizations  
(conferences, courses, publications,…)

• **pharmaceutical companies, CROs** (training of investigators; sponsoring of conferences, courses, publications; other educational activities, …; lobbying for legislation improvements, etc.)

• **scientific, professional associations/societies**  (e.g. clinical pharmacology, pharmacy, ESCI, medical ethics/bioethics, health law, etc.)

• **UNESCO**  (and many others on national or international level)

**Reasons for R/ECs collaboration and networking in Europe:**

W – E – C – S – N

• common historical experience
• similar economical, social, political problems
• common or close interests and goals  in political arena in Europe (and beyond)
• integration and harmonization efforts and initiatives underway in Europe (and beyond), incl. legislation
• effectiveness/efficacy (better results/lesser costs)
• “historical”, regional or local contacts
• scientific, economic and other interests
• personal friendships
• curiosity
• other ...

**International - Global Institutions/Organizations**

• World Medical Association [ WMA ]
• World Health Organization [ WHO ]
• CIOMS
• UNESCO
• International Conference on Harmonization [ ICH ]
• SIDCER (+ continental fora for GCP)
MISSION REPORT

THE COUNCIL OF EUROPE’S BIOETHICAL INSTRUMENTS AND PROMOTION OF RESEARCH ETHICS IN SERBIA (bilateral meeting within the framework of the Cooperation Programme to Strengthen the Rule of Law)

Author of this report Susanne Bahrke
Date 17 July 2007

Introduction

1. In collaboration with the Serbian Academy of Science and Arts and the National Committee for Bioethics of the UNESCO-Commission of Serbia, the Bioethics Division organized a bilateral meeting on ethics in biomedical research in Belgrade, Serbia. Two members of the Steering Committee on Bioethics (CDBI), Professor Elmar Doppelfeld (Germany) and Professor Jozef Glasa (Slovakia) participated in the meeting as designated European experts. Professor Elmar Doppelfeld chaired the CDBI from June 2005 to June 2007.

Objectives

2. The meeting had three main objectives:
   - to present an overview of legal standards in the field of human rights and biomedicine in Europe
   - to examine the state of implementation of fundamental ethical principles in Serbian law
   - to exchange views with the members of Research Ethics Committees

Organisation and participants

3. The organisation by the Serbian collaborators was excellent. The meeting room on day 1 was located in the centre of Belgrade at the premises of the Serbian Academy of Science and Arts, and it was well equipped and comfortable. The European experts and representatives of the Council of Europe Secretariat received a warm welcome by the members of the Committee for
Bioethics and the Serbian Academy of Science and Arts. On both days, about 40 persons attended. Participants on day 1 came from the Serbian Academy of Science and Arts, Faculties for Medicine and Biology, the Military Medical Academy (MMA), Megatrend University of Applied Sciences (private) and other science institutes. Representatives from the Ministry of Foreign Affairs and the Ministry of Agriculture attended the morning session. On day 2, a meeting had been organised in the Institute for Oncology and Radiology of Serbia with members of the Association of Clinical Research Professionals and of the Serbian Medicines and Medical Devices Agency, and members of local ethics committees.

4. Outside the programme, representatives of the Serbian Academy of Science and Arts received members of the National Committee for Bioethics of the UNESCO-Commission of Serbia, the European experts and I to exchange views on ethical issues arising from scientific developments in the medical field. On this occasion, the important role of ethics committees and the need to support their work was stressed by the representatives from all parties.

5. Photographers and journalists were present (print media, radio and television). Interviews with participants took place during coffee and lunch breaks.

6. The entire meeting was held in English, without interpretation.

**Day 1 - Opening of the meeting**

7. The meeting was opened by the president of the National Committee for Bioethics, Professor Dragoslav Marinkovic, who pointed to the long history of professional medical education and science in Serbia and academic cooperation in South-East Europe and described the activities of the National Committee for Bioethics and their interaction with COMETH and UNESCO. The Committee aims to strengthen the network of ethics committees in medical centres and universities of Serbia. Professor Marinkovic’s intervention was followed by introductory remarks by Professor Zvonko Magic of the National Committee for Bioethics, Ms Olga Cosic of the Ministry for Foreign Affairs and Mr. Denis Huber of the Council of Europe.

**Day 1 - Presentations of the speakers**

8. As the first lecturer of the day, Professor Elmar Doppelfeld of the CDBI presented the Council of Europe Convention of Human Rights and Biomedicine as well as its additional protocols and relevant EU Directives. Since biomedical research had been identified as topic of particular interest to this audience, he presented detailed information on the Protocol on Biomedical Research (CETS No. 195) that will enter into force on 1 September 2007. Questions raised by the audience concerned approval procedures for scientific research projects, the role
of sponsors, a possible obligation to publish study results where research had been performed on human beings and specific measures for the protection of healthy volunteers. Attention was also given to the subject of military research that was not regulated and that potentially raises major ethical concerns.

9. Serbian experts Professor Hajrija Mujovic-Zornic and Professor Vladislav Stefanovic presented Serbian legislation in the field of Health and Medicine as well as the work done by ethics committees at medical faculties and health institutions. The Serbian Constitution (2006) guaranteed fundamental rights and health protection and human cloning was prohibited. Health legislation was also of recent date (Health Care Act 2005) and included, for the first time, basic patients’ rights, i.e. self-determination, informed consent, privacy, the right to complain and special provisions for research on human beings. The Medicines and Medical Devices Act (2004) addressed protection of patients participating in clinical trials. Clinical trials must be authorised and respect Good Clinical Practices. The Ordinance on conditions and manner of clinical testing of medicines (2007) prescribed special protection of minors in clinical trials. A significant part of the reform process of Serbian law was the reorganisation of existing ethics committees and the establishment of local ethics committees in every clinical centre or hospital. Of particular interest was the constitution of the National Ethics Committee of the Republic of Serbia, where members nominated by the government should propose basic principles of professional ethics to health care workers, coordinate local ethical committees, monitor scientific research and clinical investigation of drugs and medical devices and give opinions in cases of dispute in the field of medical research.

The presentations were followed by a discussion on drug trials in Serbia, follow-up of Suspected Unexpected Serious Adverse Reactions (SUSAR), research ethics in medical curricula, the involvement of ethics committees in education and teaching.

10. Professor Zvonko Magic presented a study conducted in 2005 under the aegis of UNESCO-ROSTE Regional Bureau for Science in Europe, the National Bioethics Committee of Serbia and Montenegro and the Ministries of Health of Serbia and Montenegro. The study title was “Awareness of Genetic Testing in Serbia and Montenegro”, which addressed the lay public as potential user of genetic tests on one hand and general practitioners on the other hand. The aim was to estimate the general population’s willingness to participate in genetic testing and to inquire on general practitioner’s knowledge concerning use and availability of genetic testing and counselling. According to the findings, 2/3 of the lay public group were informed about the term “genetic testing”, the majority expressed willingness to be tested, but half of them did not know whether genetic tests were available for them and whether health insurance would cover testing. Of the general practitioners, about half did not give correct answers to specific questions on inheritance of diseases and did not know whether Down’s
syndrome was an inborn or inherited condition. GPs expressed lack of adequate knowledge, were not satisfied with the information they received on developments in the field of genetics and did not know where to refer patients to for hereditary predisposition testing. Most GPs supported the elaboration of protocols or guidelines for genetic testing.

11. The lectures provided the necessary background on relevant legal developments in Serbia and confirmed awareness for ethical issues amongst health professionals including researchers. The governmental institutions concerned by bioethics in Serbia are the Ministry of Health and the Ministry of Science. Signature of the Convention on Human Rights and Biomedicine (Oviedo Convention) and its additional protocol on Biomedical Research confirm that Serbia accepted fundamental ethical principles. Ratification of these texts is pending. There was only little discussion on actual challenges for researchers or ethics committee members in connection with the implementation of these texts.

**Day 2 – Opening of meeting**

12. The Director of the Institute for Oncology and Radiology, Professor Nenad Borojevic and Scientific Director, Professor Sinisa Radulovic, welcomed the Serbian participants as well as Professor Elmar Doppelfeld, Professor Jozef Glas and myself. Professor Radulovic said that the Medicines and Medical Devices Agency of Serbia received international support, in particular, from the French Health Products Safety Agency (Afssaps). The objectives of a twinning project to be conducted between 2006 and 2008 were training of Serbian agency staff at Afssaps as well as in other agencies in the countries within the European Union, creation of partnerships, facilitation of the development of infrastructure in the field of clinical trials, monitoring of adverse reactions to medicinal products, and Serbia’s entry into the international network of GMP inspectors.

**Day 2 – Presentation of the speaker**

13. Professor Jozef Glas presented the topic of clinical trials review by research ethics committees. The subsequent discussion dealt with difficulties of local ethics committees when faced with SUSARs. It was said that only a small amount of reported events actually complied with the definition of a SUSAR and clarification should be attempted as to lower the number of reports.

14. Prior to the meeting, Professor Radulovic had sent a questionnaire to the participants on the composition, role and procedures of ethics committees and asked the European experts for their opinion on the most important issues, such as the creation of new local ethics committees (currently about 20 in Serbia) and the need for a network, accreditation, independence and education of members,
quality control and external auditing, civil liability and insurance of committee members and honoraria.

**Conclusion**

15. Health legislation of Serbia is largely compliant with the provisions of relevant European treaties, in particular, in the field of pharmaceutical law and clinical testing of medicines. In some fields, there is a need to elaborate or revise specific laws, such as existing laws on artificial insemination, genetic testing, transplantation, blood transfusion, and on persons with mental disorder. There is a proposal for a specific law on patients’ rights. Furthermore, Dr Mujovic-Zornic expressed the need for Serbia to take into account European or international documents to fill in legal gaps. Support may be needed for this task.

16. The representatives of the Serbian Committee for Bioethics felt that the meeting was very valuable because it helped them to focus on certain activities of the Committee, in particular, the need to reinforce connections with the Ministry of Health and Foreign Affairs, and to effectively approach government bodies involved in legislation on bioethical issues. It was also felt, that contacts with lawyers or other experts for medical law should be improved.

17. The Serbian Committee for Bioethics proposes to publish proceedings of this meeting and they envisage further meetings with European experts on specific topics in the future.
THE COUNCIL OF EUROPE’S BIOETHICAL INSTRUMENTS AND PROMOTION OF RESEARCH ETHICS IN SERBIA

(Bilateral meeting within the framework of the Cooperation Programme to Strengthen the Rule of Law)

Belgrade, 28 - 29 June 2007

SEMINAR PROGRAMME

Venue: Serbian Academy of the Sciences and Arts, Knez Mihailova 35, Belgrade

28 June 2007

09:00 – 9:30 REGISTRATION OF PARTICIPANTS

Opening of the seminar

9:30 – 9:45 Welcome and introduction to the conference by
Representatives of the Ministry of Health and the Ministry for Foreign Affairs, Denis Huber (Belgrade office of the Council of Europe), Zvonko Magic (National Committee for Bioethics of UNESCO-Commission of Serbia)

9:45 – 10:00 Activities of the Serbian Bioethics Committee
Dragoslav Marinković, President of the National Committee for Bioethics of UNESCO-Commission of Serbia

Session 1

THE WORK OF THE COUNCIL OF EUROPE IN THE FIELD OF BIOETHICS

10:00 – 10:20 Human Rights and Biomedicine: The work of the Council of Europe in the field of Bioethics
Elmar Doppelfeld, Steering Committee on Bioethics of the Council of Europe

10:20 – 10:30 Discussion
10:30 – 10:50  Regulation of Biomedical Research – Additional Protocol “Biomedical Research” of the Council of Europe
Elmar Doppelfeld, Steering Committee on Bioethics of the Council of Europe

10:50 – 11:00  Discussion

11:00 – 11:20  Coffee Break

**Session 2**  HUMAN RIGHTS AND BIOETHICS IN SERBIA

11:20 – 11:40  Bioethics at Medical Faculties and in Health Institutions in Serbia
Vladisav Stefanović, National Committee for Bioethics of UNESCO-Commission of Serbia, Institute of Nephrology and Hemodialysis, Faculty of Medicine, University of Nis

11:40 – 11:50  Discussion

11:50 – 12:00  Review of Main Legal and Bioethical Questions and the State of Serbian Legislation
Hajrija Mujović-Zorić, Institute of Social Sciences, Belgrade

12:00 – 12:10  Discussion

12:10 – 14:00  Lunch break

14:00 – 14:20  Study of Awareness of Genetic Testing in Serbia
Zvonko Magić, National Committee for Bioethics of UNESCO-Commission of Serbia

14:20 – 14:30  Discussion

**Session 3**  THE ROLE AND ACTIVITIES OF NATIONAL ETHICS COMMITTEES

14:30 – 14:50  Role and activities of National Ethics Committees
Jozef Glasa, Slovak Medical University (SMU), Institute of Pharmacology and Clinical Pharmacology

14:50 – 17:00  Round table discussion : Interaction between the Serbian Bioethics Committee and members of COMETH
Speakers:

**Elmar Doppelfeld, MD**  
Professor, Steering Committee on Bioethics of the Council of Europe, Professor in Nuclear Medicine at the University of Bonn (Germany), Chairman of the Permanent Working Group of Ethics Committees (Arbeitskreis Medizinischer Ethik-Kommissionen in der Bundesrepublik Deutschland)

**Jozef Glasa, MD**  
Professor, Steering Committee on Bioethics of the Council of Europe, Professor at the Slovak Medical University (SMU), Institute of Pharmacology and Clinical Pharmacology, Bratislava (Slovak Republic)

**Dragoslav Marinković, PhD**  
Professor Emeritus of Genetics, Academician of the Serbian Academy of Science and Arts, President of the National Committee for Bioethics of UNESCO-Commission of Serbia

**Zvonko Magić, MD**  
Professor, Institute for Medical Research of the Military Medical Academy, Dept. for Clinical and Experimental Molecular Genetics and Genetic Engineering, Secretary General of the National Committee for Bioethics of UNESCO-Commission of Serbia

**Vladisav Stefanović, MD**  
Professor, Academician of the Serbian Academy of Science and Arts, member of the National Committee for Bioethics of UNESCO-Commission of Serbia, Institute of Nephrology and Hemodialysis, Faculty of Medicine, University of Niš (Niš, Serbia)

**Hajrija Mujović-Zornić, PhD**  
Professor, Institute of Social Sciences, Belgrade (Serbia), Research Fellow, Centre for Legal Researches

**Susanne Bahrke, Ms.**  
Bioethics Division of the Council of Europe
Opening of the Belgrade meeting

Mr. Denis Huber of the Council of Europe Office in Belgrade
Ms Olga Cosic from the Ministry for Foreign Affairs of Serbia

The meeting of the Presidency of the Serbian Academy of Science and Arts (right) with the experts from the council of Europe and members of the national committee for bioethics of Serbia
Exchange of views of the Presidency of the Serbian Academy of Science and Arts with European experts and members of the National committee for bioethics of Serbia, on bioethical issues