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Ethical issues form

A. Proposers are requested to fill in the following table

Does your proposed research raise sensitive ethical issues relating to:	YES	NO
Human biological samples	✓	
Personal data (whether identified by name or not)	✓	
Genetic information	✓	
Embryos	✓	✓

Proposers should ensure that the proposed research does not involve:

- the use of human embryos for reproductive purposes;
- the creation of human beings which could make use of their own genetic material for the purpose of research or for the production of human embryos for reproductive purposes;
- any other activity which is incompatible with the protection of human dignity and with the principles of scientific research.

National Regulations
on Ethics and Research in

Slovak Republic

Slovenskej Republike



EUR 21255



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**National Regulations
on Ethics and Research in**

Slovak Republic

Slovenskej Republike

by
Jozef Glasa

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Barbara Rhode, An Baeyens and David Coles
Brussels, 2003

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Foreword

Ethics in research is a sensitive issue, not to mention ethics in itself. Recent developments in biological and medical sciences (and not only in these fields) have put forward the tremendous potential of science, as well as the hidden risks. There is much we do not yet know about possible and unpredictable effects. Therefore, ethics has become a prominent item on the agenda of the general public, politicians and policy makers.

The main concern is now related to research on human beings, which in the Slovak Republic is regulated by legislation on biomedical research, already in force. The legislation has constantly and continually been improved and international ethical standards for biological research have been rapidly implemented.

It should be highlighted that the overall ethical standards respected in the area of biological research in Slovakia, are either identical or similar to those of the more developed European countries. At present, Slovakia is further harmonising its legislation in the field of biomedical research, research involving the use of laboratory animals and drug clinical trials, with the legislation, which is in place in the majority of European Union Member states. Relevant acts, laws and regulations are in various stages of legislative process or preparation.

Nevertheless, we are aware of the fact that the legislation backing ethics in biological research activities and its day-to-day use is a "living organism" that needs to keep up with the development of the research field. Therefore, in Slovakia, we have established a network of ethics committees in health care facilities and research institutions.

From a legal point of view, ethics committees in Slovakia are established according to the legislation in place. They are namely the Central Ethics Committee and local Ethics Committees established by directors of health care facilities or biomedical research institutions. All cases of biological research should be evaluated by ethics committees. Although an unfavourable opinion of an ethics committee might prevent the start of a potentially useful research project, allowing it to take place could lead to unforeseen risks.

Martin Fronc
Minister of Education

Introduction

The European Commission is committed to ensuring that research funded under the 6th Framework Programme respects ethical principles. What legal requirements do researchers have to respect in European Commission funded research projects?

The text of the 6th Framework Programmes makes reference to the following international texts:

- The Charter of Fundamental Rights of the European Union
- European Union directives
- Convention of the Council of Europe on Human Rights and Biomedicine (1997) and the additional protocol on the Prohibition of Cloning Human Beings (1998)
- UN Convention on the Rights of the Child (1989)
- Universal Declaration on the human genome and human rights adopted by UNESCO (1997)
- Helsinki Declaration

These regulations and texts are all well known and can be consulted on the website

http://europa.eu.int/comm/research/science-society/ethics/legislation_en.html .

Apart from such European legislation and international texts, the Specific Programme for research, technological development and demonstration 'Integrating and strengthening the European Research Area' (2002-2006) requires also that "In compliance with the principle of subsidiarity and the diversity of approaches existing in Europe, participants in research projects must conform to current legislation, regulations and ethical rules in the countries where the research will be carried out. In any case, national provisions apply and no

research forbidden in any given Member State will be supported by Community funding in that Member State.⁽¹⁾"

The specific regulation of ethical issues is a matter of subsidiarity. Rooted in the cultural background of the nation state, there are many ethical rules and guidelines in the national legal system that the scientists have to apply when conducting research in a country.

The guide for proposers of the 6th Framework Programme requires applicants to identify whether workpackages contain one or more of the five following ethical issues, namely whether the research work involves

- humans,
- human tissue,
- personal or private data,
- genetic information,
- or animal experimentation.

Detailed information on how these issues are handled has to be given, including the explanation of the applicable national legal background. Such projects that contain ethical issues may be submitted to an ethical review if they have been shortlisted after the scientific evaluation.

When co-operating in a European research consortium, it is important that researchers from partner countries have easy access to the national regulations on those five areas, where ethical issues may arise. It is an advantage if researchers not

(1) See Annex 1 (COUNCIL DECISION of 30 September 2002 adopting a specific programme for research, technological development and demonstration: 'Integrating and strengthening the European Research Area 2002-2006).

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only understand the regulation of their own countries, but also those of potential partners and when they seek to collaborate.

The Slovak text has been written by Prof. Jozef Glasa and subsequently approved by the Ministry of Education of the Slovak Republic. The Commission has been promoting this project and is now dedicating a bilingual publication (original language and English) to the accession and candidate countries in order to facilitate their participation in the 6th Framework Programme. The project has been co-ordinated for the Commission by Alexandra Bitusikova, An Baeyens and David Coles. The responsibility and credit for the contents rest with the author and the Ministry of Education of the Slovak Republic.



Barbara Rhode
Head of Unit "Ethics and Science"
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1. International instruments in Slovakian law

International treaties and conventions are part of Slovakian law through their implementation into Slovakian law, especially into the acts (laws) of the Slovakian parliament (the National Council of the Slovak Republic; in Slovak: Národná rada

Slovenskej republiky – NR SR), if ratification by the parliament is required for the conclusion of the treaty. Treaties that are contrary to the existing Slovakian law ought to be applied, except in cases where they would contravene the Constitution.

2. National overview

Overview of the national legal structure for biomedical research

Research on human beings is regulated in Slovakia by two laws:

- a) biomedical research, i.e. evaluation of new medical knowledge on man, by the Law No. 277/1994 Collection of the Laws (hereinafter referred to as 'Coll.') on health care (as later amended¹), in particular by the §40 – §44;
- b) clinical investigation of drugs, i.e. drug clinical trials, by the Law No. 140/1998 Coll. on drugs and health equipment (as later amended), in particular by the §15 – §18.

Unfortunately, more detailed regulations of both above mentioned laws are still in preparation. This explains why the formal legal basis for ethical governance of biomedical research activities in Slovakia is still rather under-developed. At the same time, however, it should be emphasised that

the overall ethical standards observed and respected (albeit often 'voluntarily') in the area of biomedical research, including those of Good Clinical Practice (GCP) requirements in the area of drug clinical trials, are identical or, at least, very close to, those of the most developed European countries.

The international ethical standards for biomedical research have been rapidly implemented into the activities of the state research funding agencies (e.g. the ethics review of biomedical research projects by ethics committees), and within the Slovakian academia and university research. Such developments were in part accelerated by external 'pressures' from foreign collaborating research centres that required a local ethical review of the proposed collaborative research projects. In the area of drug clinical trials, international pharmaceutical companies (closely followed by domestic producers) sponsoring trials require strict observance of GCP standards.

Since 1990, there have been many activities in the bioethics field in Slovakia, some of them at a distinguished international level². These include increasing awareness of the biomedical research community, contributing to 'know-how' transfer in the ethical review of research, and also creating and developing national and local structures for education, research and information in bioethics, including a network of local ethics committees in health care facilities and research institutions. The regulation of research using laboratory animals is dealt with in a specific section later on in this chapter.

At present, Slovakia is making efforts to harmonise its legislation in the field of biomedical research, including drug clinical trials with Europe. The relevant laws and regulations are pending or in various stages of preparation. (See Addendum in proofs for details on the most recent developments.)

General principles of research on humans as laid down in the Law 277/1994 on health care (as later amended)

The general provisions for biomedical research that involves human beings are laid down in Part V. – "Special Health Care" of the Law 277/1994 Coll. on Health Care (as later amended), namely in §37, 40 – 44.

In §37, the notion "special health care" comprises health care in psychiatry, health care for persons addicted to alcohol or other addictive substances, "health care connected with the evaluation of new medical knowledge on human subjects", the

removal and transplantation of tissues and organs, donation of blood and blood transfusion services.

In §40, the basic provisions concerning the "evaluation of new medical knowledge on human subjects" are given:

- definition of biomedical research, i.e. the evaluation of new medical knowledge on humans, in sub-paragraph (1), as "an investigation aiming to confirm a previously formulated hypothesis, necessary to generate new medical knowledge, new methods or hypotheses, or for clinical investigation (trial) of drugs or health aids in the interest of preservation or improvement of health of the people",
- requirement, in sub-paragraph (2), that "the research (of new medical knowledge on humans) must be preceded by laboratory experiments, experiments on animals, and a thorough evaluation of foreseeable risks and burdens for the human subjects (participating in the evaluation) in comparison to foreseeable benefits, which could arise from that evaluation",
- requirement, in sub-paragraph (3), that "before the research (of new medical knowledge on human subjects) can be started, each person involved in the evaluation must be fully informed about all medical interventions and about the risks, which might influence his/her health, and also about the objectives, methods and expected benefits arising from the research. The information must also mention his/her right not to take part in the research, or to withdraw at any time his/her consent to participation in the evaluation without this having any negative impact (on the health

care provided to him/her). The information and consent of the patient must be recorded in his/her health documentation.”,

- provision, in sub-paragraph (4), that “the research (of new medical knowledge on humans) is reviewed, commented upon, and authorised by the health care facility (where it is planned to be performed) in collaboration with professional organisations (such as the Slovakian Medical Chamber), which establish for this purpose an independent committee for review of ethical questions relating to that research (referred to hereinafter as the “ethics committee”),
- provision, in sub-paragraph (5), that “an integral part of the evaluation (of new medical knowledge on human subjects) is to draft a protocol of the study, which should contain the proposal and description of the research procedures to be performed, as well as description of any ethical problems connected with the research. The research protocol should be submitted for review, comments and approval to the ethics committee, when the ethics committee so requires. The person responsible for the research is obliged to provide all information required by the ethics committee for the follow up of the evaluation.” (NA³: The “protocol” should be understood here both as a document to be submitted to the ethics committee and the health care facility’s director in seeking the approval/authorisation of the research, as well as the documentation of the research conducted after the approval/authorisation. The actual language, however, is to be specified (and harmonised with the relevant international

standards) within the pending revision of the law).

- definition, in sub-paragraph (6), that “within the experimentation (of new medical knowledge on human subjects) (both categories), distinction should be made between experiments with therapeutic purposes, and experiments without therapeutic purposes”,
- provision, in sub-paragraph (7), that “research (of new medical knowledge on human subjects) should not be performed, if the life or health of persons participating in the evaluation would be threatened or at risk. If, during a study, a threat to a person’s health occurs, the research should be stopped immediately”,
- distinction, in sub-paragraph (8), that “the evaluation (of new medical knowledge on human subjects) does not include medical interventions that in specific cases might save the life of a patient in imminent danger, even if these may not yet be established treatments (‘lege artis’ methods)”.

In §41, the conditions for conducting research (of new medical knowledge on man) for therapeutic purposes are stipulated:

- definition, in sub-paragraph (1), research (of new medical knowledge on human subjects) for therapeutic purposes, which is to be referred to as “the evaluation of a new therapeutic method on a patient suffering from a disease (illness, condition), which the study is aimed at, where a better outcome of the treatment of that disease (illness, condition) is expected (in the patient), or if

the objective of the evaluation is of diagnostic or therapeutic benefit to that patient”,

- provision, in sub-paragraph (2), that “research (of new medical knowledge on humans) for therapeutic purposes can only be performed after the written or otherwise documented consent of the fully legally competent patient has been obtained. In the case of minors or persons not fully legally competent, the evaluation can only be performed after consent of their legal representative has been obtained, which can only be given on recommendation of the professional consultation (NA: “Professional consultation” refers to an expert group of physicians, provided for by law or ministerial regulation, which reviews and evaluates the health status of the person concerned and gives recommendations concerning the possible course of action to be taken from the medical point of view.)

In §42 – 43, the conditions for conducting research (of new medical knowledge on humans) without therapeutic purposes are stipulated:

- definition, in §42 sub-paragraph (1), of the evaluation (of new medical knowledge on humans) without therapeutic purpose, which is to be referred to as “the evaluation of a new therapeutic method or a new drug on a healthy person or on a patient suffering from a different disease (illness, condition), than the one that is the subject of the research. Its aim is not to achieve any diagnostic or therapeutic benefit for the persons taking part, but rather to evaluate the new preventive, diagnostic, or therapeutic method or drug, or to obtain new medical knowledge for the progress of medical science”,
- requirement, in §42 sub-paragraph (2), that “the evaluation (of new medical knowledge on human subjects) without therapeutic purpose can only be performed after the written or otherwise documented consent of the person, who must be over 18 years of age and fully legally competent, has been obtained”,
- prohibition, in §42 sub-paragraph (3), of “the evaluation (of new medical knowledge on humans) without therapeutic purpose ... on
 - a) pregnant women, b) minors and persons deprived of full legal competence, c) human embryos and fetuses, d) persons detained or imprisoned, e) persons in military service (regular or substitute) or civil service, f) foreigners”,
- “conditions (in §43), under which research (of new medical knowledge on humans) without therapeutic purpose can be performed only if :
 - a) the research has a clear objective, justification and is based on all relevant previous theoretical and clinical knowledge;
 - b) the new medical knowledge and development of the new method is necessary for society and cannot be achieved by other means;
 - c) the evaluation has been preceded by successful laboratory research, either by laboratory animal research, or by other successful scientifically proven data;
 - d) it can be assumed that the expected benefits of the research will exceed the foreseeable risks for the persons taking part in the study);
 - e) it can be assumed that neither death, nor permanent impairment of health, or

unfavourable personality changes would appear as a result of the research;

- f) the physical, psychological burdens and constraints placed on the person taking part in the research are restricted to the absolute minimum.”

In §44, the requirements concerning the responsibility of the health facility in the case of any study-related damage to the person taking part in the research, as well as the obligation of the health facility to take out an insurance policy for this purpose is stipulated:

- in sub-paragraph (1): “the health care facility is responsible in the case of any study-related damage to the person taking part in the research”,
- in sub-paragraph (2): “the health care facility performing the study is obliged to take out a specific insurance policy for covering the cases of any study-related damage to the persons taking part in the research”.

The principles of drug clinical research as laid down in the Law 140/1998 Coll. on drugs and health equipment

The principles governing the clinical investigation of drugs (drug clinical trials) are laid down in the Law No. 140/1998 Coll. on drugs and health equipment (as later amended¹), in particular in §15 – §18.

In §15, the principles of a drug clinical evaluation are given:

- sub-paragraph (1) defines the objectives of a drug clinical investigation, as “an evaluation of

therapeutic efficacy of the investigational product, its relative safety,...revealing contra-indications,... interactions,... adverse reactions,... and obtaining new scientific knowledge”,

- sub-paragraph (2) concerns the authorisation of the institutions/departments, where the conduct of drug clinical evaluation is allowed; the specific authorisation is issued by the State Institute of Drug Control (SIDC); in Slovak – Štátny ústav pre kontrolu liečiv (ŠÚKL), in as far as the institution/department fulfils the appropriate material, technical and personnel requirements for the conduct of the clinical drug trials, and also meets the requirements of Good Clinical Practice (GCP),
- sub-paragraph (3) contains a definition of GCP and provisions concerning detailed regulation 1 relating to the clinical investigation of drugs and GCP to be issued by the Ministry of Health (NA: At present this regulation is still pending),
- sub-paragraph (4) provides that “the clinical evaluation of drugs for human use is performed on a healthy or an ill person”, and “the clinical evaluation of drugs for veterinary use is performed on a healthy or an ill animal”, the relevant general provisions concerning the research on human beings as given in the Law No. 277/1994 Coll. on health care (NA: See above), and concerning the research on animals as given in the Law No. 115/1995 Coll. on the protection of animals, and of the Law No. 337/1998 Coll. on veterinary care (as later amended) are also cited here (NA: For details see the section on research on animals),

- sub-paragraph (5) contains the condition that "the clinical evaluation of a drug can only be allowed when the experts of the SIDC issue a positive opinion with regard to the results of its pharmaceutical and toxicological-pharmacological evaluation"; and it also contains the requirement of specific authorisation for the conduct of phase I and III trials that has to be issued by the SIDC on behalf of the Ministry of Health (the Commission for New Drugs of the ministry); whereas phase IV trials (NA: "postmarketing trials") are only to be reported to the SIDC before their commencement,
- in sub-paragraph (6) to sub-paragraph (8), a description of phase I - including the provision for including the patients in "justified instances" - phase II and phase III drug clinical trials (in humans and in animals),
- sub-paragraph (9) contains a description/definition of phase IV drug clinical trials, which is referred to as a clinical investigation of a drug that is performed after market authorisation has been issued by SIDC, and that aims at finding new information about therapeutic effects, adverse effects, contra-indications and interactions of the drug used within the framework of the therapeutic indications registered,
- sub-paragraph (10) sets the requirement that drug samples for clinical investigation should be marked as such.
- in sub-paragraph (1) the provision that authorisation is issued by the SIDC upon application of the sponsor; thereby a definition of sponsor is also provided,
- in sub-paragraph (2) the application requirements are listed, these include: detailed information on the drug, its producer, the sponsor, a report on the results of the drug pharmaceutical and toxicological-pharmacological trials, a report on results of any previous clinical investigations of the drug, evidence of the registration of the drug in another country/countries, protocol (plan) of the trial, evidence about the authorisation given by the SIDC to the institution/department where the clinical trial is to be performed, an information leaflet to be given to the trial participants (subjects), the opinion of the ethics committee of the institution/department where the clinical trial is to be performed,
- sub-paragraph (3) contains provisions concerning the authorisation issued by the SIDC,
- in sub-paragraph (4) it is stipulated that the clinical trial could only be started within the 12 months following the date on which the authorisation was issued by the SIDC, after this time period the authorisation expires,
- sub-paragraph (5) entails provisions concerning the abrogation of authorisation of the trial previously given by SIDC, where new risks to the health of the trial participants are revealed, or where there is non-compliance with the legal provisions.

In §16, the principles, basic requirements, and the procedure to obtain authorisation of a drug clinical investigation by the SIDC are described:

In §17, the obligations of the sponsor are listed, and in §18 those of the (principal) investigator are enumerated.

Provisions concerning the clinical evaluation of medical devices and health equipment are given in §27, sub-paragraph (7) – (12).

Ethics committees

The first document devoted to ethics committees was published by the Ministry of Health of SR (MH SR) in June 1992, entitled "Guidelines for the establishment and work of ethics committees in health care facilities and research institutions"⁴. These guidelines, which at the time of their publication were quite progressive and comprehensive, will soon be replaced by the specific and detailed regulations of the MH SR as mentioned above (the regulation on clinical investigation of drugs and on GCP; the regulation on ethics committees).

At present, from the legal point of view, ethics committees in Slovakia are established according to the requirements of either:

- a) §40 par. (4) of the Law No. 277/1994 Coll. on health care – for ethics committees to review biomedical research projects; or
- b) §16 par. (2) sub-paragraph j) of the Law No. 140/1998 Coll. on drugs and health equipment¹ – for ethics committees to review protocols of drug clinical trials.

The requirements set in the laws mentioned above are rather general and simple. Local ethics committees themselves, however, and the health

care facilities and research institutions, when establishing and developing these bodies, respect the relevant international requirements and standards (especially those of the GCP) as reflected in the ethics committees' statutes and standard operating procedures (SOPs)⁵ on a voluntarily basis. The laws cited do not explicitly define "the competencies" of ethics committees in the ethical governance of research. The Law No. 140/1998 Coll. on drugs and health equipment¹ in §16 merely states that "an opinion of an ethics committee of the facility where the clinical drug investigation is to be performed is required", while the Law No. 277/1994 Coll. on health care in §40 par. (4) requires that "the health care facilities (that review, comment and approve the clinical investigations) (...) should establish independent committees for review of ethical questions (ethics committees). An ethics committee monitors the performance of clinical investigations, has at least 3 members and is composed of health care professionals and at least one lawyer. Excluded from membership of the ethics committee is: any person, who has ordered the investigation; any person who is close to, or an employee of the former person; and any researcher. Any decision by the committee requires the consensus of all its members."

In practice, the unfavourable (negative) opinion of an ethics committee is able to prevent the realisation of a research project (or drug clinical trial) in a given health care facility or biomedical research institution (or stop it; especially in the case of non-compliance or serious adverse events). It does not automatically exclude, however, its realisation in another institution in Slovakia, if the

ethics committee of another institution - although quite improbable nowadays - were to give a favourable opinion on the same research protocol. Such cases, with the exception of some specific ethical issues (e.g. those relevant for catholic health care facilities), will be very rare in the future, as a result of the networking, education and information-sharing that is being developed for ethics committees according to the new concept elaborated by the Central Ethics Committee (CEC) of MH SR in June 2002.

Types of ethics committees present or foreseen in the Slovak Republic

The following types of ethics committees are established or anticipated in Slovakia:

- a) Central Ethics Committee (CEC) of the Ministry of Health
The CEC has been established by the Minister of health as an advisory body on questions of bioethics, including those connected with ethics of biomedical research and clinical trials. This committee only exceptionally performs the ethical review of projects or protocols for a specific research project (when, for example, there is no other relevant or responsible ethics committee for the specific project). The establishment and activities of CEC are governed by the statutes and working procedures issued by the Minister of health.
- b) (Local) Ethics Committees ((L)ECs)
LECs are established by directors of health care facilities or biomedical research institutions to

review protocols of clinical trials or biomedical research projects planned to be performed in that facility/institution, and to provide a follow up of the research protocol approved.

- c) Regional Ethics Committees (RECs)
The RECs have not yet been established, but they are foreseen according to the Directive 2001/20/EC⁶. Their task will be to review and follow up multicentre clinical trials and multicentre biomedical research projects (with the exception of the review of the 'local aspects' of research projects).

As mentioned above, more detailed provisions concerning LECs (and new provisions on RECs) will be laid down by the pending regulations to be issued by the Ministry of health and will relate to ethics committees, clinical trials and GCP.

It is expected that in the future, LECs established within health care facilities will also function as so-called 'clinical ethics' committees. The other possibility is that some health care institutions would establish two types of local ethics committees – 'research' and 'clinical ethics' committees.

What kind of projects or procedures should go to ethics committees for approval?

All biomedical research projects, as defined in the Law No. 277/1994 Coll. on health care in §40 subparagraph (1), i.e. "investigation aimed at confirmation of a previously formulated hypothesis, which is necessary for obtaining new medical knowledge, elaboration of new methods or hypotheses, or for clinical investigation (trial) of

drugs or medicinal devices or health equipment in the interest of preservation or improvement of people's health", should be "reviewed, commented upon and approved by the health care facility" (§40 sub-paragraph (4), while ethics committees should be used to review ethical questions relating to research.

Moreover, an "opinion on the clinical trial given by the ethics committee of the facility, where the clinical trial is to be performed," is required by §16 sub-paragraph (2), sub-paragraph j) of the Law No. 140/1998 Coll. on drugs and health equipment as a

necessary document to be submitted by the sponsor to the National Institute for Drug Control (NIDC) (to its Commission on New Drugs) together with the application for the clinical trial authorisation. In practice, both applications for a clinical trial authorisation (required for phase I - III drug clinical trials), and for the notifications (sent to NIDC) required for phase IV clinical trials, should contain a favourable opinion of the ethics committee. Thus, the sponsor should seek the favourable opinion of the ethics committee before submitting the application to the NIDC.

3. Research involving persons

As mentioned in the previous section, the provisions concerning the research on human beings (i.e. "evaluation of new medical knowledge on human subjects") in general, and those related to informed consent of persons taking part in the research in particular, are contained in §37, 40 - 44 of the Law No. 277/1994 Coll. on health care (as later amended). In this context, more general provisions regarding the consent of any patient undergoing a health care procedure or an intervention apply (as given in §13 of the same law), as well as those provisions dealing with the information to be provided to the patient before consent is sought (§15). In §6 sub-paragraph (2) let. d), the right of the patient to refuse his/her participation in the research is stipulated. The most important provisions will be repeated, or commented upon below as relevant for this part of the paper.

Requirements for informed consent

The requirements for informed consent to be given by a person, or a patient for any health care procedure or intervention are given in §13, 15 of Law No. 277/1994 Coll. on health care.

These are as follows:

- in §13 sub-paragraph (1), any health care intervention or procedure can only be carried out with the consent of the patient,
- in §13 sub-paragraph (2), the physician is obliged to obtain consent from the patient prior to any serious diagnostic or therapeutic procedures or interventions,
- in §13 sub-paragraph (4), the consent of a legal representative, or guardian, or foster parent on

- behalf of a minor, or a patient with a limited legal capacity, or a patient without legal capacity is required (includes the possibility to consent for a minor over 16 years of age or a patient with a limited legal capacity, who – according to the physician – is able to decide about the intervention/procedure concerned),
- in §13 sub-paragraph (5), upon the recommendation of a "professional consultation" consent must be given by a legal representative, guardian, or foster parent on behalf of a minor, a patient with a limited legal capacity, or a patient without legal capacity, for any particularly serious health care procedure or intervention, or intervention capable of seriously affecting the future life of the patient (this includes the possibility to consent for a minor over 16 years of age or for a patient with a limited legal capacity, who is able to decide about the intervention/procedure concerned; as well as the possibility for the health care facility to seek the decision of a court, if the legal representative, or guardian, or foster parent does not consent to the intervention or procedure recommended by the "professional consultation"),
- §13 sub-paragraph (6), contains an exception to the explicit consent requirement: a necessary emergency therapeutic intervention is permitted (in the patient's best interest), even if the consent of the patient, his/her legal representative, or authorisation of the court or "professional consultation" (NA: See above) cannot be obtained in due time (this provision, however, cannot be automatically applied for "emergency" research),

- §15 deals with the duties of a physician regarding the necessary information (either "full" or "appropriate") that they have to provide to the patient regarding the health care provision.

The requirements for the informed consent of a person, or patient in the context of research are given in §41 and 42 of Law No. 277/1994 Coll. on health care:

- in §41 sub-paragraph (2): "the evaluation (of new medical knowledge on human subjects) with therapeutic purposes (NA: i.e. "therapeutic research".) can only be performed after the written, or otherwise documented, consent of the adult and fully legally competent patient has been obtained. Minors or not fully legally competent persons can only be involved in the evaluation after the consent of their legal representative has been obtained, which must have been given following the recommendation of the professional consultation (NA: "Professional consultation" refers to an expert group of physicians, provided for by the law or ministerial regulation, which reviews and evaluates the health status of the person concerned and gives recommendations concerning the possible course of action to be taken from a medical point of view.),
- in §42 sub-paragraph (2): "the evaluation (of new medical knowledge on humans) without therapeutic purpose (NA: i.e. "non-therapeutic research".) can only be performed after the written, or otherwise documented, consent has

been obtained from the person over 18 years of age and fully legally competent".

§16, sub-paragraph (2), let. j) of the Law No. 140/1998 Coll. on drugs and health equipment sets out detailed requirements for the information to be provided to human subjects participating in a drug clinical trial before they give their consent to participate in the trial. The information should include: information about the trial, its goals, possible benefit(s) for the participant, possible risks and burdens, other treatment options, confidentiality of the participant's personal data, the possibility to withdraw consent and to end participation in the trial at any time, how to do so and its consequences for the human subject concerned.

Legally competent, but vulnerable research subjects

The Law No. 277/1994 Coll. on health care (as later amended) contains a prohibition, in §42 sub-paragraph (3): namely the evaluation (of new medical knowledge on human subjects) without therapeutic purpose (NA: i.e. "non-therapeutic research".) ... on the following vulnerable groups: a) pregnant women, b) minors and persons deprived of full legal competence, c) human embryos and fetuses, d) persons detained or imprisoned, e) persons in the military (regular or substitute) or civil service, f) foreigners. Although the law contains no specific provisions with regard to "evaluation (of new medical

knowledge on human subjects) with therapeutic purposes" (NA: i.e. "therapeutic research"), the law does not seem to prohibit the performance of this type of research on the groups mentioned above in as far as the ethics committee's approval and the health care facility director's authorisation have been obtained, and if all other relevant provisions of the law apply.

The same seems to hold true for patients in psychiatric institutions where there is the possibility to involve them in non-therapeutic and therapeutic research.

There are no specific legal provisions concerning research involving nursing mothers.

4. Research involving human biological material (blood, organs, tissues, cells, DNA)

Provisions with regard to the removal of human biological material (tissues or organs) for transplantation or research purposes can be found in Law No. 277/1994 Coll. on health care (as later amended), namely in §45 – §47. These paragraphs are relatively brief and general. However more detailed legislation on these issues is pending.

In §45, the basic provisions for the removal of human tissues or organs from live or dead donors are given:

- sub-paragraph (1), the removal of tissue or organs should only be performed in health care facilities and research institutes authorised to do so by the Ministry of Health; the authorisation is subject to requirements and provisions described in the law,
- in sub-paragraph (2), any organ or tissue removed at a medical intervention must undergo a biopsy by a qualified professional,
- in sub-paragraph (3), a definition is given of the living and the dead donor, and the requirement is stipulated that tissues or organs can only be removed from the donor for transplantation, treatment or research purposes,
- sub-paragraph (4), contains a definition for the recipient of the tissue or organ.

Laws regarding use of biological material from live patients

The requirements applicable to the removal of tissues or organs from living donors (usually understood as a donor giving his/her organ for transplant in another patient – recipient; but these

could be applied also to research, when all other relevant provisions of the law apply) are described in §46, namely:

- the donor, who must be legally competent, must give his/her informed consent in writing and this can be withdrawn at any time before the removal of the tissue or organ (sub-paragraph (1);
- a review of the case by the “professional consultation” is required (NA: See above) before the removal of the tissue or organ can be authorised; the removal of the tissue or organ is prohibited if there is a serious health risk for the donor notwithstanding the fact that the donor has given consent in writing or if the donor is in prison (sub-paragraph (2);
- “any removal of a tissue or organ from a living donor can only be performed in a state-owned health care facility authorised for doing so by the Ministry of Health”; the facility should take an insurance policy to cover any damage to the living donor (that may occur in connection with the removal of the tissue or organ) (sub-paragraph (3),
- full information on any health risks involved must be provided to the donor when seeking his/her consent (sub-paragraph (4),
- any financial gain for the donor is prohibited.

There are no specific provisions in the law regarding research using human tissues or organs removed from living donors.

Laws regarding the use of biological material from deceased persons

The rules applicable to the removal of tissues or organs from deceased donors (usually for their transplantation to another patient – recipient, but these could also be applied to cases of research, when all other relevant provisions of the law apply) are given in §47, namely:

- sub-paragraph (1), that the removal of tissue or an organ from a deceased person is only allowed, if that person has not previously objected to such a donation by making a written statement or by a statement made in another conclusive form (the so-called presumed consent), and is forbidden if such a statement of the deceased person is available; the statement should be part of the deceased person's health documentation;
- according to sub-paragraph (2), review of the case by "professional consultation" is required (NA: See above.) before authorisation can be given for the removal of the tissue or organ and the identity of the deceased person must be proven;
- sub-paragraph (3), any financial gain in connection with the removal and use of the tissues or organs from a deceased donor is prohibited.

There are no specific provisions in the law for research using human tissues or organs from deceased donors. (NA: see comments above.)

Laws regarding old collections of biological material, pre-existing and ongoing research

Up until now, no specific legal provisions exist in Slovakia for research using human biological material from already existing collections. Nor are there any provisions for extending the goals and scope of the research using human biological material for which consent has been previously given by the donor or his/her legal representative, but for purposes other than the planned research.

With reference to recital 26 of Directive 98/44/EC - is consent required for patents developed from or containing human biological material?

At present, there are no specific legal provisions in Slovakia concerning patents developed from or containing human biological material, neither for the consent of a donor of such material.

5. Research involving human embryos and embryonic stem cells

How is the embryo defined?

There is no specific definition of human embryo given in Slovakian law. However, an embryo is usually referred to as a human being following the completion of fertilisation of a human egg by a human sperm until the end of the 12th week of its subsequent development. After that the human being is referred to as a foetus.

Can human embryos be used for research?

Research "without therapeutic purpose" (i.e. the so-called non-therapeutic research) on human embryos and fetuses is prohibited by the provision contained in §42 sub-paragraph (3) let. c) of the Law No. 277/1994 Coll. on health care.

On the one hand, as there are as yet no other specific provisions regarding research on human embryos contained in existing Slovakian legislation, it can be presumed that in some strictly defined instances research "with therapeutic purpose" (i.e. the so-called therapeutic research, or research aiming to provide a benefit to the embryo concerned) may be allowed under the present law. More detailed legislation on these issues is pending. It will have to be in line with the relevant provisions of the Convention on human rights and biomedicine (Oviedo, 1997), which was ratified by Slovakia in 1998.

On the other hand, legislation in this area is lacking at present and the performance of medically assisted reproduction centres in Slovakia is almost solely regulated by their internal operational guidelines and ethical codes. It may be assumed,

however, that some research on human embryos within the framework of infertility treatment is performed.

What are permitted sources of embryonic stem cells?

No specific legal provisions regarding the sources or research on human embryonic or adult stem cells exist in Slovakia so far. Some legislation on the matter may be expected soon, however. At present, the use of living human embryos for harvesting the stem cells for research purposes would be prohibited (under the provision of §42 sub-paragraph (3) let. c)).

Laws regarding human cloning

Slovakia signed and ratified (in 1998) the additional protocol on the prohibition of the cloning of human beings (Paris, 1998) to the Convention on human rights and biomedicine (Oviedo, 1997).

Cloning of a human being is prohibited by §46a of the Law No. 277/1994 Coll. on health care, which quotes the wording of the Protocol. Whereas the provision given in the law does not make any distinction between the so-called therapeutic and reproductive cloning, and whereas §42 sub-paragraph (3) let. c) of the same law prohibits research "without therapeutic purpose" (i.e. the so-called non-therapeutic research) on human embryos and fetuses, it is understood that "therapeutic cloning" is also prohibited under the existing law.

Moreover, the recently revised Slovakian Penal Code (Law No. 140/1961 Coll., as later amended) defines in §246a "any intervention aiming to create a human being in any stage of its formation, which is genetically identical to another human being whether living or dead" as a penal offence. Thus, the actual wording seems to cover both types of human cloning (i.e. the "reproductive" and

"therapeutic" ones). Punishment would include imprisonment for 3 to 8 years, a financial penalty, and the injunction of professional activities. The penalties would increase, if the offence is committed in the setting of an organised crime, or when the perpetrator has made a major financial gain, or a major damage has ensued.

6. Personal data

The provisions concerning the protection of personal data are given in the Law No. 428/2002 Coll. on the protection of personal data. The law, which amended the previous legislation on this matter (namely the laws No. 52/1998 Coll. and No. 241/2001 Coll.), transposes the relevant international instruments on personal data protection (including the Directive 95/46/EC⁷) into the legal system of Slovakia. The most important provisions of the law, relevant in the context of biomedical research, will be listed or commented on below. For further details, the reader is referred to the text of the law itself.

The provisions concerning personal data protection and processing contained in law No. 428/2002 should be adhered to in connection with relevant provisions of law No. 277/1994 Coll. on health care concerning personal health data and information (confidentiality, protection, consent for processing, revelation to third parties, exemptions provided for in law, etc.).

How is personal data defined?

The definition of personal data is given in §3 of the Law No. 428/2002: "data concerning an identified or identifiable physical person, while such a person is the person, who can be identified directly or indirectly by using a generally used identifier, or by using one or more characteristics or signs, that comprise his/her physical, physiological, psychological, mental, economic, cultural, or social identity."

§4 gives explicit definitions of other important notions used in the law: sub-paragraph (1), let. a) personal data processing, b) provision of personal data, c) provision of access to personal data, d) making

personal data public, e) liquidation of personal data, f) imposing a block on personal data, g) information system, h) purpose of personal data processing, i) consent of the person, j) transborder flow of personal data, k) anonymised data, l) address, m) general identifier, n) biometric data, o) audit of the information system safety; sub-paragraph (2) operator, sub-paragraph (3) intermediary, sub-paragraph (4) authorised person, sub-paragraph (5) the person and sub-paragraph (6) the user.

Regulatory approach to data rendered anonymous

The definition of anonymised data is provided in §4 sub-paragraph (1) k) of the law: "data transformed in such a way that they cannot be attributed to the person concerned." There are no further specific provisions in the law concerning the anonymised data with the exception of the provision in §7 sub-paragraph (4) b) (consent of the person is not required) "if personal data are processed for statistical purposes, then those data must be anonymised").

Fundamental rights and privacy

The detailed specific provisions to protect the rights of the persons with regard to their personal data processing are contained in the 3rd Chapter of the Law No. 428/2002. These are e.g. the right to require information from the operator about one's own personal data that are processed and stored, the right to require correction(s) and/or updating of one's data, destruction of the data when the purpose of their processing no longer exists, or when

there has been a violation of the law, the right to ask for a copy of one's personal data that were processed by the operator; the right to object to the processing, use or provision of one's personal data for direct marketing activities and the right to object to the transfer of one's personal data abroad.

The purpose of the law, as mentioned in §1 subparagraph (1) is to provide: a) the protection of personal data of physical persons, b) principles for the processing of personal data, c) safety of personal data, d) the protection of the rights of persons with regard to the processing of their personal data, e) principles for transborder flow/transfer(s) of personal data, f) registration of the information systems, g) establishment of the governmental office (authority) for the protection of personal data.

However, there are several important provisions contained in other chapters of the law that deal with protection of the rights and personal interests of the individual, whose personal data are processed (i.e. collected, catalogued, stored, elaborated, provided, etc.). The following examples may be listed here:

- provisions regarding the conditions under which personal data can be processed (Chapter 1), namely in §5 the rights and obligations of the operator and intermediary (the only legal or physical persons allowed to process the personal data); in §6 the purpose of personal data processing; in §7 the consent of the person, whose personal data are to be processed (and exceptions for the situations, when obtaining the consent of that person is not possible or necessary), detailed provisions are given in subparagraph (1) – (14) of this paragraph; in §8 special categories of personal data (data revealing ethnic or racial origin, political views,

religion or world views, membership of political parties or movements, trade unions, health data and data on sexual life) that are generally not allowed to be processed, unless under specific conditions or exemptions provided for in the Law No. 428/2002 (especially in §9) or other relevant legislation; in §10 collection/acquisition of personal data; in §11 truthfulness of personal data; in §12 accuracy and topicality of personal data, corrections and updating; in §13 destruction of personal data;

- provisions concerning safety of personal data (Chapter 2), including the provisions concerning confidentiality (§18);
- provisions on the transborder flow of personal data (Chapter 4).

Conditions for data processing

The provisions concerning the conditions under which personal data can be processed are given in Chapter 1 of the Law No. 428/2002. They are elaborated on in greater detail in §5 - §14 (as listed in the previous section of this paper). However, they are to be understood in connection with other relevant provisions described in other chapters of the law, as these elaborate on some specific issues in greater detail.

The following conditions are the most important for personal data processing to be allowed according to the law:

- the operator and the intermediary for personal data processing must be defined (legal or physical persons meeting the criteria provided for in the law and thus allowed to legally process personal data - §5);

- the purpose of personal data processing must be clearly specified (§6);
- the consent of the person, whose personal data are to be processed, must be obtained and appropriately documented; the exceptions, where obtaining consent is not possible or necessary, must be dealt with, if applicable, according to the detailed provisions given in the law (§6, sub-paragraph (1) – (14));
- the exceptions concerning the special categories of personal data (ethnicity, race, political/religious/philosophical views or convictions, membership of political parties, movements, or trade unions, health data and data on sexual life) should be respected (§8 – 9);
- the procedures used in personal data processing should meet the criteria required by the law (§10 – 14).

Description of any regulations that are not in the Directive on Data Protection but which the directive allows and identification of any regulations which are contrary to the Directive

The provisions of the Law No. 428/2002 should be in accordance with the requirements of the Directive 95/46/EC.

What exemptions from data protection law are there for research?

In general, the personal data of the participants (subjects) of the biomedical research must be strictly protected against their unauthorised publication or

misuse by any third party. The authorisation for use and even publication of personal data is to be given solely by the person concerned (in special circumstances by his/her legal representative, or his/her relative (for deceased persons).

The rare exemptions from these general requirements are provided for by various relevant laws, if the rights or important interests of other individual(s), or of the society (e.g. serious public health issues, serious threats to health or life(-ves) of other person(s), etc.) come into conflict in a particular case.

The Law No. 428/2002 itself provides for an exception concerning further processing of data beyond the original purpose "for historical, statistical or scientific purposes" (§6 sub-paragraph (1) a), and also, in §7 sub-paragraph (4) a), "... (the consent of the person not required)... if personal data are processed solely for the purposes of creation of scientific, art, or literary works..., ...as well as for historical or scientific purposes, without the possibility that these data will be made public and as long as the data processing is performed by the operator to whom the data were attributed in connection with his work area."

Altogether, despite the legislation concerning personal data protection in Slovakia (Law No. 428/2002) being fully in accordance with the relevant international standards (including the Directive 95/46/EC), it is expected that with the forthcoming revision of the Law No. 277/1994 Coll. on health care, some more specific wording on personal health data will be added to the relevant sections with regard to biomedical research.

7. Genetic information

In Slovakia, there is no specific law on human genetics. However, important and relevant legal rules were adopted in the field of personal data protection – the Law No. 428/2002 Coll. on protection of personal data. (NA: See the previous section of the paper.)

Moreover, insofar as genetic information may be considered to be an integral part of the personal health information, several relevant provisions of the Law No. 277/1994 Coll. on health care do apply, in particular those contained in

- §6 sub-paragraph (2) – the specific rights of persons who receive health care, including, amongst others, “the right to respect of one’s physical and psychological integrity; the right for the confidentiality preservation (by health care professionals) concerning all data on the person’s health status, and concerning all facts relating to his/her health (if the law does not provide otherwise); the right to decide about the person’s participation in health research”;
- §15 The information for the patient, in sub-paragraph (8), the following provision is given: “In the case of a serious genetic disease, or a suspicion of its transmission, the physician gives information about the possible disease to the patient and to his/her blood relatives, if he assumes that they could transmit the disease further to their offspring. The person, who has received such information from the physician, is obliged to keep this information confidential. The physician should inform that person about this obligation.”
- §16 The health care documentation contains provisions regarding access (and its limitations) to the personal health documentation for the patient him/her-self, the health care providers, state authorities, courts, attorneys, legal representatives, etc. The protection of confidentiality of personal health information and patient’s privacy should always be maintained; exceptions applicable in certain serious circumstances are provided for directly in the law.

8. Research involving animals

In general, research involving animals is regulated in Slovakia by the relevant provisions contained in two laws, namely, the Law No. 115/1995 Coll. on the protection of animals and the Law No. 337/1998 Coll. on veterinary care (as later amended by laws No. 70/2000 and No. 23/2002). These laws impose appropriate conditions for the breeding, keeping, transport, humane treatment, etc., of research animals, and for avoiding any misuse, abuse or mistreatment. Both laws are quoted in other legislation concerned with animal experimental research, especially in the Law No. 140/1998 Coll. on drugs and health equipment (§14 Toxicological - pharmacological studies, §50 Clinical investigation of veterinary drugs).

Animal ethics committee structure, role and remit

Ethics committees to review research projects to be conducted on animals are not yet provided for by Slovakian law. The first national guidelines on ethics committees⁸ published in 1992 provided for these committees "to be established by the directors of health care facilities and research institutions, where this is necessary". Otherwise, local research ethics committees are also supposed to review animal research protocols.

However, in several research institutions, animal research ethics committees were established during the previous decade, usually by directors of these institutions, to comply with relevant international standards and requirements. Some pressures from the public (especially from the activists of

environmental or animal protection NGOs) have also contributed to these developments.

Where such committees exist, they are expected to review and follow up all research being planned or conducted on animals in their institutions, using as reference points international documents relevant to the problems encountered. They are also expected to satisfy themselves, within the review and follow up of the research, that the conditions of keeping and any treatment of the research animals is in compliance with the provisions of the Law No. 115/1995 Coll. on the protection of animals and the Law No. 337/1998 Coll. on veterinary care (as later amended).

Application of the "3Rs" (reduction, refinement, and replacement)

The application of "3Rs" principles is considered to be a good scientific practice in animal research in Slovakia. The principles are not explicitly mentioned in the existing legislation, but they are implicitly contained in relevant provisions of the Law No.

115/1995 Coll. on the protection of animals, such as – in §26 sub-paragraph (1) – "experiments on animals may only be conducted after it has been proven that at the present state of knowledge the necessary data cannot be obtained by other methods, (the experiments) should be conducted in the necessary scale only, and for the purpose of a) prevention, study or treatment of the diseases of human beings or animals, b) advancement of the knowledge of non-pathological structures, functions and reactions of human beings or animals, c) study of the

- environmental pollution, d) evaluation of the safety of chemicals or products for the health of human beings or animals, or their efficacy against pests, e) production of sera, vaccines, drugs, or other biological materials, f) education in the field of medicine and natural sciences, pharmacology or veterinary medicine”;
- in §27 let. e), “...(requirement)... to adequately plan the experiments,... to use appropriate methodologies,... to reduce the number of experimental animals used....”.

Identification of animals, which can and cannot be used for research

There are no explicit provisions concerning the prohibition of use of particular animals in experimental research. However, §25 of the Law No. 115/1995 Coll. on the protection of animals provides that “experiments may be conducted as a rule (usually) on laboratory animals”, i.e. (§24 sub-paragraph (3) on “the animals bred solely for research or scientific purposes in the facilities authorised to do so according to the requirements of §31 let. a) of the Law No. 115/1995.” Also gravid animals are specifically mentioned in the law as requiring special protection (e.g. no transport allowed, if they might be expected to give birth during that time (§3 sub-paragraph (2), etc.).

Regulations regarding research purposes for which animals may or may not be used

The use of animals in experiments for the tobacco industry, decorative cosmetics and detergents is

prohibited under §26 sub-paragraph (2) of the Law No. 115/1995 Coll. on the protection of animals. The exception, provided for by this law, is compulsory testing required by the Law No. 272/1994 Coll. on protection of the health of the people.

Regulations on keeping and using (conditions under which they are kept; what happens to them after experimentation)

Provisions concerning keeping and using laboratory animals are given in the Law No. 115/1995 Coll. on the protection of animals. The laboratory animals could only be bred, kept and used for research purposes in the facilities authorised according to §31 a and b. The authorisation is issued (and withdrawn) by the state veterinary service. The research animals (§27 d) “should be provided with the appropriate care (nourishment, drinks, microclimate, veterinary care), they “should be bred appropriately and in compliance with conditions of good laboratory practice”. “Research animals and animals excluded from the experiments should be killed without suffering, anxiety and disproportionate pain.” (§27 f)

Use of transgenic animals

There is no specific legislation on the use of transgenic animals in Slovakia.

Addendum in proofs

An important amendment of the Law No. 140/1998 Coll. on drugs and health equipment was passed by the National Council (NC) of Slovakia on December 3, 2003. It was published in the Collection of laws of SR as the Law No. 9/2004 Coll. (Coll., part 5, 2004, p. 62 – 76) and shall enter into force on February 1, 2004 (with the exception of §16 sub-paragraph (3), §20 sub-paragraph (1) c), and §49 – these shall enter into force on the day of entering into force of the agreement btw. SR and EU on the entering of SR into the EU).

The most important changes introduced into the Law No. 140/1998 could briefly be summarised as follows:

- §1: new sub-paragraph (2) was added: “(2) By this law the legal acts of the European Community listed in the (new) Enclosure 4 of the Law No. 140/1998 Coll. are taken.” The Enclosure 4 lists the following acts:
 - Directive 2001/20/EC of April 4, 2001,
 - Directive 2001/82/EC of November 6, 2001 (with exception of the Enclosure I),
 - Directive 2001/83/EC of November 6, 2001 (with exception of the Enclosure I),
 - Art. 1 – 5 of the Directive 89/105/EEC.
- §15 was given a new title: “General provisions on clinical drug investigations”. In this paragraph, several sub-paragraphs were re-formulated in accordance with the language of the Directives mentioned above, namely sub-paragraph (1) – definition of a drug clinical investigation, sub-paragraph (3) – definition of Good Clinical Practice, sub-paragraph (4) – referring to other Slovak Republic legal norms governing clinical research in humans and in animals (see respective parts of this report for details), sub-paragraph (5) – definition of phase I studies as non-therapeutic biomedical research, phase II – IV studies as therapeutic biomedical research, sub-paragraph (10) – requirement that a sponsor, or its appointed representative should have a seat in the Slovak Republic. New sub-paragraphs were added to §15, namely sub-paragraph (11) – definition of the (principal) investigator, (12) – definition and requirements concerning the protocol, (13) – requirements concerning the informed consent of the research subject, (14) – prohibition of any trial seeking to modify the genetic identity of the research subject.
- new §15a - §15c were added after §15: §15a – Protection of subjects, §15b – Protection of minor subjects, §15c – Protection of legally incompetent subjects who are not minors,
- new wording was introduced for §16 – Opinion on ethics of the clinical investigation, namely: sub-paragraph (1) the request for an opinion on ethics of the clinical investigation is submitted to the ethics committee by the sponsor, sub-paragraph (2) lists the items a) – 1) the ethics committee is looking into when reviewing the protocol of the clinical trial, sub-paragraph (3) the provision that the ethics committee can ask for additional information from the sponsor only once, sub-paragraph (4) time limits for the ethics committee issuing the opinion: 60 days from receiving the request for the opinion when reviewing the protocol, 35 days when reviewing the change in the protocol (protocol amendment), sub-paragraph (5) extension of the time limits to 90 days (or, exceptionally, for another 90 days,

- when the ethics committee gives reasons for such an extension) in the cases of protocols to investigate gene therapies, somatic cell therapies, or using genetically modified organisms (GMOs), sub-paragraph (6) no time limits for issuing the ethics committee's opinion in the case of trials of xenogenic cell therapies, sub-paragraph (7) "single opinion" in the case of multicentre clinical research; the ethics committee issuing the opinion upon the request of the sponsor (who should for his part indicate that it is a multicentre clinical trial) is obliged to refer its opinion to the ethics committees of all other participating centres before issuing it,
- new §16a - §16h were introduced after §16, namely: §16a – Permission for clinical (drug) investigation/trial (a long paragraph containing ten detailed sub-paragraphs), §16b – Suspending and prohibition of the clinical trial, §16c – Database on clinical trials, §16d – Production, import, labelling and storage of the trial product or trial drug, §16e – Inspections of Good Clinical Practice and Good Manufacturing Practice by the State Institute for Drug Control, §16f – Reporting of serious adverse events, §16g – Reporting of serious adverse effects (reactions), §16h – Documentation storage,
 - new wording was introduced for §17 – Obligations of the sponsor (a long paragraph containing fourteen detailed sub-paragraphs), §18 – Obligations of the investigator (contains eleven detailed sub-paragraphs),
 - new §18a – Non-interventional clinical trial (investigation) was introduced after §18; gives definition of the non-interventional clinical trial, which refers to a study of a drug in clinical practice after marketing authorisation for this drug has been issued and the following conditions are met: a) the drug is prescribed according to the conditions given in the marketing authorisation decision, b) inclusion of the particular subject in any therapeutic strategy aim of the study is not done according to the protocol, but is done according to established principles of therapeutic practice, c) the decision of the doctor to prescribe the drug and the decision to include the patient in the investigation are separated, d) no additional diagnostic or monitoring procedures are used, e) epidemiological methods are used for the analysis of the data obtained.

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