Acta Clin Croat 2019; 58:497-507
doi: 10.20471/acc.2019.58.03.14

Review

INFORMED CONSENT IN CROATIAN CLINICAL LABORATORY PRACTICE – CURRENT ISSUES AND FUTURE PERSPECTIVES

Iva Sorta-Bilajac Turina[1,2] and Vesna Šupak Smolčić[3,4]

[1]Department of Social Medicine, Teaching Institute of Public Health of Primorje-Gorski Kotar County, Rijeka, Croatia; [2]Department of Environmental Medicine, School of Medicine, University of Rijeka, Rijeka, Croatia; [3]Clinical Department of Laboratory Diagnostics, Rijeka University Hospital Centre, Rijeka, Croatia; [4]Department of Medical Informatics, School of Medicine, University of Rijeka, Rijeka, Croatia

SUMMARY – This paper deliberates on the place and role of informed consent in everyday clinical laboratory practice. Taking into account international ethical guidelines such as the UNESCO Universal Declaration on Bioethics and Human Rights, the Declaration of Helsinki of the World Medical Association, and Croatian national laws and codes such as the Act on the Protection of Patients' Rights, the Act on Medical Biochemistry, the Code of Ethics of Medical Biochemists and Medical Deontology, the Act on Healthcare Services, and the Code of Ethics of the Croatian Chamber of Healthcare Workers, an overview is given on the actual implementation of the aforementioned recommendations and regulations. A distinction between consent to a medical procedure and consent to enrolment in a research protocol is strongly stressed out. Special emphasis is placed on the role of specialists in laboratory medicine and masters of medical biochemistry in the process of obtaining informed consent. The design of an 'informed consent interview' is to be taken into consideration. Additional deliberation is needed on the option of 'broad consent'. It is concluded that informed consent should represent an important and routine activity within Croatian clinical laboratories.

Key words: *Informed consent; Biochemistry; Clinical laboratory services; Croatia*

Introduction

Informed consent is a current clinical reality, both in treatment and research. However, the clinical reality is constantly changing, particularly under the influence of new technologies. Therefore, the key issues from the period of the 'birth of bioethics' are nowadays a memento of a romantic time when the ethical component of medicine managed to keep pace with its professional-technical component. Informed consent, both as a theoretical value and as clinical practice, developed precisely from the vortex of time. It was rooted in the 'achievements' of Nazi medicine, hovering for years over any research protocol as a silent admonition that 'it should never happen again'. The cradle of informed consent is the Nuremberg Code, which developed from the Nuremberg trials against Nazi physicians in 1947. Its first point was that "the voluntary consent of the human subject is absolutely essential"[1]. Other points indicate that:

- the experiment should aim at positive results for society that cannot be procured in some other way;
- it should be based on previous knowledge (such as animal experiments) that justifies the experiment;
- it should be designed to avoid unnecessary physical and mental suffering;

Correspondence to: *Prof. Iva Sorta-Bilajac Turina, MD, PhD,* Department of Social Medicine, Teaching Institute of Public Health of Primorje-Gorski Kotar County, Krešimirova 52a, HR-51000 Rijeka, Croatia
E-mail: iva.sorta-bilajac@zzjzpgz.hr
Received March 8, 2018, accepted October 30, 2018

- it should not be conducted when there is any reason to believe that it implies a risk of death or disability;
- it should put the risks in proportion to the expected benefits;
- procedures and facilities must be provided that adequately protect participants against the experiment's risks;
- researchers must be scientifically trained and qualified;
- participants must be free to quit the experiment at any point when they feel physically or mentally distressed; and
- researchers should stop the experiment at any point when they observe that continuation would be dangerous[1].

The concept of informed consent first appeared in conducting research, which is a logical sequence. One might even call it 'a burdened legacy'. In clinical medicine (in terms of treatment, not trial), informed consent has long been reserved only for the most controversial interventions and procedures that have been considered 'ethically exotic'[2], balancing thereby between centuries of paternalism ('physician-father' knows best) and a shy entrance of the patient's rights through the back door of medicine. Today, however, "decision-making and participation in decision-making process about one's own health is recognized as the patient's human right"[3].

The definition of informed consent evolved over time "from the narrow focus on the physician's or researcher's obligation to disclose information about the quality of a patient's or subject's understanding of information and his right to authorize or refuse a biomedical intervention"[4]. This refers to an authorized action by the physician/researcher towards the patient/subject. The concept is quite simple, "the physician cannot treat the patient before he/she presents him/her with the basic information about the treatment and proposes an alternative procedure. The patient then decides what treatment he/she wishes to be applied to him/her, or if he/she wants for any treatment to be applied at all"[3]. What needs to be pointed out is that the "right to refuse the proposed medical procedures is only the flip side of the right to giving consent and together they form a unity", which emphasizes the patient's/subject's position of an 'autonomous agent'[3].

Informed consent is derived from two (bio)ethical principles, i.e. the traditional (hippocratic) principle of beneficence and the contemporary principle of autonomy[5]. Acting as the denominator of the two, at first glance conflicting principles, i.e. the physician's obligation to make the care for the patient his top priority and the patient's right to express his/her own will even though it may be contrary to the physician's advice[5], informed consent has importantly changed (i.e. it is continuously changing) the relationship between physicians and patients. This opens up space for practical application of informed consent, i.e. "it roots the consent, that is, it gives the right to the protection of autonomous choice", ranging from individual patients to participants of scientific research[6]. In accordance with the principle of autonomy (*voluntas aegroti suprema lex*), every patient has the right to make independent decisions about his/her health and disease, about acceptance or refusal of the medical interventions proposed, even about his/her stay in a medical institution, etc., assuming that he/she is capable of independent decision-making[5]. However, it is necessary to point out the difference between:

- general autonomy – institutional guidelines and protocols (i.e. social rules of consent) which define the legal and institutionally valid consent for all potential patients or subjects in a scientific research; and
- personal autonomy – autonomous and informed authorization to conduct a medical intervention or participation in a study related to each individual (which is expressed through the autonomy of consent/choice, i.e. the right of approve/refuse and/or the right to choose)[5].

Precisely, the clinical laboratory services are located at the very crossroads of these two 'subtypes' of autonomy. That is why healthcare professionals (as well as patients) often find themselves in a confusing situation where they are simply not sure whether it is necessary to request an informed consent for a particular procedure, or if it can be derived from institutional protocols which this procedure is subject to. So, do we even require an informed consent in the laboratory? If so, what kind? Specialized or conclusive? Written or oral? Who 'gives' and who 'receives' it? What does it mean to 'give' or 'receive' consent for a laboratory diagnostic test?

International (Bio)ethical Guidelines

In the medical-ethical-legal sense, informed consent is in the clinical laboratory field directly or indi-

rectly regulated by a number of international guidelines, as well as national laws and regulations. If we understand ethics as "a spotlight that illuminates the empirics"[7], then the UNESCO Universal Declaration on Bioethics and Human Rights, and in particular the Declaration of Helsinki of the World Medical Association (WMA) constitute the starting point for discussion on these issues. They represent a kind of superstructure, or supra-national medical-ethical-legal constructs, which serve as a foothold for derivation of national laws regulating the field of biomedicine and healthcare, and by-laws such as codes of individual professional chambers. When analyzing these documents, the notion should always be kept in mind that a consent or refusal of consent to a diagnostic or therapeutic procedure should not be equated with agreeing to participate in research.

The Universal Declaration on Bioethics and Human Rights was adopted by the 33rd General Conference of UNESCO in 2005. This Declaration "addresses ethical issues related to medicine, life sciences and associated technologies as applied to human beings, taking into account their social, legal and environmental dimensions (...). Human dignity, human rights and fundamental freedoms are to be fully respected (…). The interests and welfare of the individual should have priority over the sole interest of science or the society (…)"[8]. One of the aims of this Declaration is "to recognize the importance of freedom of scientific research and the benefits derived from scientific and technological developments, while stressing the need for such research and developments to occur within the framework of ethical principles set out in this Declaration and to respect human dignity, human rights and fundamental freedoms"[8]. The issue of informed consent is discussed in Articles 6 and 7.

The Declaration of Helsinki of the WMA was adopted at the 18th general meeting in 1964 and supplemented several times. It represents "a statement of ethical principles for medical research involving human subjects, including research on identifiable human material and data"[9]. The Declaration is addressed primarily at physicians, but the WMA "encourages others who are involved in medical research involving human subjects to adopt these principles"[9]. Some of the Declaration's General Principles referring to the topic are: "Medical research is subject to ethical standards that promote and ensure respect for all human subjects and protect their health and rights (…). It is the duty of physicians who are involved in medical research to protect the life, health, dignity, integrity, right to self-determination, privacy, and confidentiality of personal information of research subjects. The responsibility for the protection of research subjects must always rest with the physician or other healthcare professionals and never with the research subjects, even though they have given consent"[9].

Croatian Normative Framework

The Act on the Protection of Patients' Rights (APPR) was adopted in 2004 and revised in 2008. This Act "defines the rights of patients when using healthcare, as well as the way to protect and promote those rights. The patient, in terms of this Act, shall mean any person, sick or healthy, who requests or who is undergoing certain measures or services for the purpose of preserving and improving health, preventing illness, treatment or medical care and rehabilitation"[10]. This Act guarantees to every individual, as the patient, "the general and equal right to quality and continuous healthcare, appropriate to his/her state of health, in accordance with the generally accepted professional standards and ethical principles, in the best interest of the patient, with respect to his/her personal views"[10]. The principles of humanity and accessibility are respected in the provision of healthcare services. The basic rights that this Act regulates are the following: the right to co-decide (which includes an exception to the right to co-decide, the right to information, the right to refuse receipt of the information, the right to accept or refuse a medical procedure or treatment, and the right to protection of the patient who is unable to consent), the right to confidentiality, privacy, and access to medical records, the right to maintenance of personal contacts, the right to arbitrary abandonment of healthcare institutions, as well as damage compensation. It also regulates the implementation of interventions in the human genome. The right to the protection of participants in scientific research is especially emphasized[10]. Informed consent is regulated by Articles 6 through 21.

The Act on Medical Biochemistry (AMB) was adopted in 2003 and revised in 2008. It regulates the principles, organization, and carrying out of activities in the field of medical biochemistry. It relies on "con-

stant efforts to maintain and raise the quality of medical and biochemical services in the interest of the health of the patient; the respect for the patients' rights, the promotion of a dignified, responsible and professional conduct of a Master of Medical Biochemistry; and the adherence to the rules of the profession and the Code of Ethics of Medical Biochemists and Medical Deontology"[11].

The Code of Ethics of Medical Biochemists and Medical Deontology (CEMBMD) was adopted in 2009 at the third session of the Chamber. The Code emphasizes that it is "a medical biochemist's honorable duty to devote his/her profession to the health and well-being of man. A medical biochemist shall show a high degree of humanity and provide all available laboratory services equally to all regardless of particularities such as age, sex, race, nationality, religion or political belief, economic or social status and personal relationship with the user, thereby respecting human rights and dignity of the person. Abiding by the principles of the Code, a medical biochemist shall observe, maintain and improve the moral and professional level of medical biochemistry"[12]. It is important to point out that, regarding research, the Code builds on the Declaration of Helsinki, to which it directly refers (Article 18 of the Code)[12].

The Act on Healthcare Services was adopted in 1987 and revised in 2009. It refers to the services provided by sanitary engineers, healthcare related radiological-technological services, occupational therapy, and medical-laboratory services. Services of medical-laboratory diagnostics are most commonly performed in a team whose head is the appropriate specialist in laboratory medicine or master of medical biochemistry. The Act defines the standard of education, the need for further training, the conditions for carrying out activities, and the duties and responsibilities of healthcare professionals. Particular emphasis is placed on the duty of carrying out services by applying the best professional knowledge, respecting the principles of medical ethics and the Code of Ethics of the Croatian Chamber of Healthcare Workers, the duty to respect the rights of patients, and the obligation to keep a professional secret[13].

The Code of Ethics of the Croatian Chamber of Healthcare Workers (Code of Ethics and Deontology of Sanitary Engineering, Healthcare Radiological and Technological Services, Occupational Therapy, and Medical-Laboratory Services) was adopted in 2012. It contains a system of values and rules of professional conduct of healthcare workers, who are obliged to adhere to in their professional work. Among other things, the Code prohibits discrimination and emphasizes respect for the rights and dignity of every person, provides an honorable, competent, responsible and quality service, and protects the patient's or user's information from other persons, the employer, and the wider community about the healthcare procedure and/or service being performed. It also describes the relationship with other healthcare workers and the profession, and emphasizes the respect of competences. Particular attention is paid to participation in research and publication of scientific papers[14].

Informed Consent in Croatian Clinical Laboratory Practice

The question that directly arises in practice seems at first glance to be a very logical one: do we need to conduct an 'informed consent interview'[5] every time when a patient comes to draw blood? Is the physician's referral, which the patient brings to the laboratory, a form of consent to the laboratory procedure[12]? A comparison and interpretation of international and national medical-ethical-legal guidelines can be found in Table 1. When analyzing the displayed normative framework, it can be concluded that specialists in laboratory medicine and masters of medical biochemistry, as well as bachelors of medical laboratory diagnostics and medical laboratory technicians should be involved in the process of informed consent, given that this is not merely the signing of such a form, but a concrete and important everyday clinical and, obviously, laboratory practice. The following considerations and proposals are designed while keeping in mind the current Croatian clinical reality, but considering the approach to the problem through international ethical guidelines.

All the abovementioned healthcare professionals are invited to safeguard and promote the right of patients/health service users/research subjects to confidentiality and privacy. They also participate in the protection of personal medical data[15]. Since clinical laboratory services deal with the analysis of biological material (blood, urine, cells, tissue, cerebrospinal fluid, etc.), attention should be paid to the protection of

personal data. Specifically, the protection of medical personal data occupies a special place within the framework of the protection of personal data. Data on a person's health status are very important and they belong to specific data that require strict standards, which regulate the access to such information with regard to authorized persons and under certain conditions[16]. It should be borne in mind under what conditions and in what circumstances may the data on the health status of a person be available, and how the patient's personal data can be protected to the best extent possible[16].

The right to information is a prerequisite for the right to accept/refuse medical treatment or research. In order to counteract the debate about what information should be provided, to whom, how, and who should provide it[17], the creation of information materials has been proposed, which would be available to patients/subjects in their preparation for a particular medical procedure/research involving laboratory tests. In this way, the patient will have the opportunity in an environment unburdened by time restrictions to study all the relevant information and be autonomously able to ask questions. This contributes to the promotion of the 'health literacy'[18] of patients/users/subjects who thus become more active participants in the process of giving-receiving informed consent.

If a patient comes to the laboratory with a physician's referral for laboratory testing, having such a referral is treated as written consent[12], and an 'informed consent interview' need not be further implemented. If a patient-client comes to the laboratory without a referral (i.e. at their own request, with the obligation of a financial compensation for the service), it is in accordance with the principles of 'good laboratory practice' to conduct an interview of informed consent. It is the obligation of all healthcare professionals to enable access to medical information, but it is within the obligation of specialists in laboratory medicine and masters of medical biochemistry to deliver such information to the patient. In this case, it is also suggested to create sets of informed consent forms for particular sets of tests.

Genetic testing is a separate topic, and because of the specificity of test subjects (individuals, relatives and descendants can be seen as a group patient), it requires a more detailed approach, but it is clear that there must be a previously obtained patient's/user's informed consent[19]. So, some laboratory procedures cannot be categorized as a 'conclusive agreement', but for them the patient must give a separate consent[17]. Resolving the issues of the (non)possession of informed consent to a genetic testing (but it could also be applicable to other testing) before arrival of the patient/user to the laboratory would greatly facilitate daily work. Following the model of Mayo Medical Laboratories, it is recommended to define the list of tests that would require from patients/clients to have written informed consent already on file, obtained from their physician[20].

Testing for human immunodeficiency virus, hepatitis, etc., may pose a problem if the patient/user with full capacity of consent does not want to receive information on the outcome of the test result. Then the medical biochemist acts in accordance with Articles 14 and 15 of the APPR because they refer to cases where the patient/user must be aware of the nature of their disease, so as not to endanger the health of others. A notification is then given to the 'surrogate', and if there is a referral pursuant to Article 10 of the Code of Ethics, then the patient's/user's physician, who has recommended the testing, will be immediately notified[10,12].

Finally, for each medical procedure, except for cases of medical emergencies, it is necessary to obtain informed consent in writing (e.g., a referral). Giving an oral or combined consent in laboratories is usually not the case, except for people with disabilities who have requested the testing themselves. Also, in accordance with the principles of medical law, a patient/user can always refuse to submit to a diagnostic testing, unless he/she thereby threatens the health of others[8,10,12]. In that case, bachelors of medical laboratory diagnostics and medical laboratory technicians are obligated to immediately notify the head of the team (specialist in laboratory medicine or master of medical biochemistry)[13].

Since medical research in a laboratory is carried out using identifiable human material or data, such as research on material or data contained in Biobanks or similar repositories, the medical biochemist and medical laboratory technician (MLT) must seek a written informed consent for the collection, storage and/or reuse for epidemiological, demographic or other scientific purposes[9,12]. The possibility of an oral and combined consent, i.e. a lack of necessity for consent in the case of emergencies, cannot be applied in research. In

Table 1. Interpretation of the normative framework of informed consent in medical biochemistry and clinical laboratory practice

	International ethical guidelines		Croatian ethical framework				
	UNESCO Declaration on Bioethics and Human Rights	Declaration of Helsinki	Act on the Protection of Patients' Rights (APPR)	Act on Medical Biochemistry (AMB)	Code of Ethics of Medical Biochemists and Medical Deontology (CEMBMD)	Act on Healthcare Services (AHS)	Code of Ethics of the Croatian Chamber of Healthcare Workers (CECCHW)
Privacy, confidentiality and protection of personal data	Article 9	Article 24	Articles 25, 28	Article 18	Articles 2, 6, 7,10	Articles 55, 65, 66	Articles 7, 9
	Confidentiality and privacy stand out in all documents as the fundamental rights of patients/subjects/users, and it is emphasized that the obligation to maintain and implement these rights lies with health professionals and institutions. All documents, with the exception of the Declaration of Helsinki, touch upon the current issue of the protection of personal medical data, with particular attention being paid to the amount of data and the purpose of data collection.						
			APPR and AMB refer to regulations on the protection of personal data and records in the field of healthcare (such as the Act on the Protection of Personal Data), while CEMBMD further draws attention to the problem of the accessibility of data due to computerization in the healthcare system[10-12]. AHS uses a more general formulation of 'keeping a professional secret'. It highlights the responsibility of maintaining proper documentation and data truthfulness[13]. The Chamber of Medical Biochemists recognizes the importance of respecting the ethical and legal framework of manipulating medical data. Therefore, it has proposed a Statement of Obligation to Respect the Principles of Ethical Behavior, and mentions, among others, the obligation to protect confidential information obtained in the course of one's professional activities and to prevent their misuse[15]. CECCHW describes in detail the procedures for protecting the privacy of healthcare service users, from the conditions and patterns of sampling to the protection of the systems transmitting, processing, and storing data for the purpose of preventing misuse. The amount and purpose of information about the user of the services, which the healthcare worker needs to collect, are very clearly defined. Everything he/she learns in the course of his/her work is considered a professional secret. According to the regulations, violation of secret is a punishable offence. The healthcare service user has the right to confidentiality, access to his/her medical data, and to choose who is entitled to information about his/her health[14].				
Informed consent to medical treatment	**Right to information**						
	/	/	Articles 8-15	/	Article 10	/	Articles 3, 6, 7, 12
			The first problem one faces is that the legislator, in the case of medical treatment, has not specified which information should a healthcare professional give to the patient/user of healthcare services, but they are very specifically stated in the context of the protection of patients' rights[17]. Article 8 of APPR stresses that patients have the right to be completely informed about the following: "- their health, including medical assessment of the results and outcomes of a particular diagnostic or therapeutic procedure, - recommended examinations, procedures and planned dates of their performance, - potential benefits and risks of performance or non-performance of examinations and procedures, - their right to decide on the recommended examinations or procedures, - possible alternatives to recommended procedures, - the course of procedures when provided healthcare, - further course of provided healthcare, - recommended lifestyle, and - health insurance rights and procedures for exercising those rights"[10]. CECCHW provides in very general terms that every user of the service, among other things, has the right to information, informed consent, and health counseling[14]. It is emphasized in Article 9 of the APPR that "notifications referred to in Article 8, paragraph 1 of this Act shall be provided upon the patient's verbal request by a healthcare worker with a university degree, who directly provides the patient with some form of healthcare service"[10]. This would mean that upon the patient's request, a specialist in laboratory medicine (SLM) or master of medical biochemistry (MMB) is obliged to give the patient all the information about the state of his/her health and specifically in connection with the type of sample and analysis he/she is conducting[10]. In addition, in accordance with Article 10 of the CEMBMD, a SLM/MMB "should warn about unnecessary analyses and refuse to implement those which in his/her conviction and expertise are unacceptable, unethical or harmful to patients. He/she can and should advise the patient/user and/or the physician to conduct additional measurement procedures if he/she in his/her expert knowledge believes they will be useful… A SLM/MMB shall ensure that, in case of a requirement for a particular interpretation, test results are not communicated directly to the patient without the opportunity for an appropriate consultation… A SLM/MMB cannot provide a diagnosis"[12].				

Table 1. Continued

		According to CECCHW, a healthcare professional legally authorized to provide information should provide the patient/user of the service with sufficient information to enable him/her to make a decision about his/her health and well-being. In doing so, he/she must be accurate, i.e. provide accurate information about the nature of the service being provided, as well as the relevant time limits and financial charges[14]. A bachelor of medical laboratory diagnostics and medical laboratory technician should not provide a diagnosis, suggest therapy, or interpret the results to the healthcare user. He/she may independently reach conclusions and solutions within the diagnostic procedure in accordance with his/her competences[14]. According to Article 13 of PPRA, "the right to information is also granted to the patient with an impaired ability to reason, in accordance with his/her age, physical, mental and psychological condition"[10]. In accordance with Articles 14 and 15 of PPRA, "the patient has the right to refuse, by means of a written and signed statement, to be informed about the status of his/her health and the expected outcome of the proposed and/or performed medical procedures and measures"[10]. However, "the patient with a full legal capacity cannot waive the right to information in cases in which he/she must be aware of the nature of his/her illness, so as not to endanger the health of others"[10]. In this case, "he/she has the right to appoint in writing or in any other credible way a person who will be informed instead of him/her. The patient has the right to be informed even when his/her consent is not a condition for starting a treatment"[10]. Article 10 of the CEMBMD is referred to in case of the patient's refusal to receive a notice based on which a SLM/MMB "should perform laboratory tests in accordance with the degree of urgency and immediately inform the physician who has recommended the testing to the patient/user about the findings of critical values"[12].
	Right to accept/refuse a treatment	
	Articles 5-7 /	Articles 16-18 / Articles 3, 4 Article 69 Articles 3, 4
	Through Articles 5-7, the UNESCO Declaration places the term in the context of the principle of autonomy, and emphasizes that any preventive, diagnostic and therapeutic medical intervention must be preceded by a free and informed consent of the individual (which can at any time be withdrawn without consequences). National legislation shall apply to people who are not capable of giving consent, but maximal involvement in the decision-making process is recommended[8]. The Declaration of Helsinki does not address the issue of consent to a medical treatment, except that the General Principles call for the International Code of Medical Ethics: "A physician shall act in the patient's best interest when providing medical care"[9].	APPR deals very extensively with the issue of informed consent. Firstly, it defines the right to co-determination as a combination of the right to information and the right to accept or refuse a particular diagnostic or therapeutic procedure. Article 16 states that "the patient has the right to accept or refuse a particular diagnostic or therapeutic procedure (by means of a written statement), except for cases of urgent medical interventions without which the patient's life and health would be endangered or permanent damage would be caused to his/her health"[10]. People with disabilities may do this by means of a notarial act or an expressed statement before two witnesses about a 'surrogate'. For patients who cannot express their consent because of their condition, legal incapacity or minority, the consent is given/refused by the 'surrogate' in accordance with Article 17, apart from cases of urgent intervention (Article 18)[10]. CEMBMD simplifies the situation for the practice and each arrival at the laboratory with a physician's referral or request for a test is understood as giving consent for all procedures carried out on the subject, with a breakdown into younger and older juveniles (up to and above the age of 16, taking into account the need for a parent's, guardian's or companion's consent, except for an emergency), as well as people with limited freedom[12]. It is important to note that the Code uses the formulation 'service user' or 'subject', even in this segment which describes the "relationship with the patient/service user". This highlights a foothold in the Declaration of Helsinki, as specified in Article 18[12]. What the nomenclature is concerned, it is important to note that in APPR, the term 'ill person' has been changed to 'patient' as late as in the revision of 2008 (because "the patient is considered every person, sick or healthy, who requests or who is undergoing a certain measure or services...")[10]. According to CECCHW, a healthcare professional shall respect the right of a mentally capable and conscious citizen/patient/user to self-determination, which implies that he/she as a well-informed individual is involved in making decisions on the procedure, freely accepts, interrupts or refuses the recommended procedure, refuses the services of a particular healthcare worker, and asks for a second opinion. For all actions, the patient/user must give consent in conscious and aware state of mind. Rejection of the procedure must be respected and documented[14]. According to AHS, in case the patient deliberately refuses the suggested diagnostic procedure, a bachelor of medical laboratory diagnostics or medical laboratory technician must immediately inform the head of the team (a SLM/MMB)[13]. CECCHW, similar to CEMBMD, recognizes the elderly and younger minors, and, in case of the latter, the service shall be conducted with the consent of the parent or legal guardian or adult closest family members accompanying the child, except for emergencies. If an older minor (16-18 years) comes with a physician's referral requesting a medical test or procedure, the signed referral will be considered as the parent's written consent. CECCHW alternately uses the terms 'citizen', 'service user' and 'patient'. In some future revision, one might think about consolidating the terminology.

Table 1. Continued

<table>
<tr><td rowspan="5">Ethical aspects of research</td><td>Articles 6, 7</td><td>Articles 25-32</td><td>Articles 19-21</td><td>/</td><td>Article 18</td><td>Article 65</td><td>Articles 13, 14</td></tr>
<tr><td colspan="7">The UNESCO Declaration, the Declaration of Helsinki, the APPR and the CECCHW define in very complex terms that the participation in scientific/medical research should be voluntary. It can only be carried out with “the prior, free and informed consent of the person concerned. The confidentiality of data related to the research participants, as well as their safety and well-being must be ensured by becoming familiarized with all potential risks and outcomes. The information should be adequate, provided in a comprehensible form and should include modalities for withdrawal of consent…”[8].
CEMBMD states adherence to the recommendations of the Declaration of Helsinki and its revisions, which is a very general formulation. In practice, it leaves room for different interpretations! Clarification is given by defining the duties of SLM/MMB in scientific research with the aim of “protecting the life, health, privacy and dignity of patients. The well-being of the individual takes precedence over the interests of science”[12].
AHS very broadly defines the duty to respect the rights of patients, the principles of medical ethics, and the CECCHW[13].</td></tr>
<tr><td colspan="3">The Declaration of Helsinki states in great detail the contents of medical information. “After ensuring that the potential subject has understood the information, the physician or another appropriately qualified individual must then seek the potential subject’s freely-given informed consent, preferably in writing. If the consent cannot be expressed in writing, the non-written consent must be formally documented and witnessed”[9]. Special attention is paid to subjects in a dependent relationship with the physician (which is an almost everyday occurrence in research carried out in hospitals).</td><td colspan="4">Unlike the Declaration of Helsinki, APPR explicitly allows only the written form of informed consent (a much more rigid formulation of consent to a medical treatment of the same Act)[10]!
According to CECCHW, any participation in research must be substantiated by the subject’s/healthcare user’s written consent. There is also a need for written consent when publishing any (medical) data that determine the patient/user. It is interesting that participation in research is directly linked to educational activities and it is explicitly required that the patient/user give his/her consent, in written form, even during participation in educational activities[14]!</td></tr>
<tr><td colspan="7">Both Declarations and APPR explain and allow the circumstances of including a ‘surrogate’ in place of those incapable of giving consent due to their condition, work incapacity or minority[8-10]. In contrast to the consent to medical intervention, in regard to research there are no possibilities for exemption in cases of emergencies[8-10].</td></tr>
<tr><td colspan="3">The obligation to obtain consent in cases of manipulation with human material and/or data should be emphasized, whereby the Declaration of Helsinki and the CEMBMD have agreed positions. The Declaration of Helsinki in Article 32 notes in detail that “for medical research using identifiable human material or data, such as research on material or data contained in biobanks or similar repositories, physicians must seek informed consent for their collection, storage and/or reuse. There may be exceptional situations where consent would be impossible or impracticable to obtain for such research. In such situations, the research may be done only after consideration and approval of a research ethics committee”[9].</td><td colspan="4">CEMBMD, in turn, states that “the results of laboratory tests, which are separate from the identification of the patient, may be used for other purposes, such as epidemiological, demographic or other scientific purposes”[12], whereby informed consent is not specifically mentioned. However, since the Code builds on the Declaration, it should be concluded that providing consent is nevertheless necessary. As suggested by the Declaration, in cases where this is impossible, for example, in studies in which the already existing material is being re-used, this time for a different purpose, the approval of the Ethics Committee of the healthcare institution and/or the medical faculty is required[9,12], which has already been the practice of scientific research in Croatia.</td></tr>
</table>

Table 1. Continued

Disciplinary responsibility	/	Articles 41, 42	Articles 17, 29	Article 21	Articles 67, 71, 77, 83	Articles 18-23
	As for disciplinary responsibility, these clauses are not mentioned in the Declarations as being international (above-national) guidelines, but it is left to the implementation at the national medical-legal level.	It is necessary to point out that violations of duties and services are stressed out in all documents analyzed, differing in the extent of treating the topic, whereby APPR is the most detailed document. Articles 41 and 42 of APPR envision fines for institutions or individuals if they deny the patient the right to information, the right to accept or refuse a particular diagnostic or therapeutic procedure, who act in violation of the rights of the 'surrogate', who carry out scientific research on patients in violation of Articles 19-21 (governing the protection of the patient being submitted to research), violate the right to confidentiality of data, and refuse to disclose information (which a healthcare professional with a university degree, who directly provides some form of health service, is required to provide the patient with) (Article 9)[10], whereby the latter is directly related to SLM/MMB. AMB generally relates to the disciplinary responsibility, covering it through articles 17 and 29, which refer to a temporary or permanent revocation of licenses for independent work. The approval shall be revoked temporarily if, for example, it is determined that a SLM/MMB "endangers the health and lives of patients through his/her work"[11]. Members of the Chamber are responsible for serious and less serious breaches of duty and reputation whereby "any violation of the duty, reputation and the CEMBMD that carries more weight regarding, for example, the vulnerability of the patient" is considered a serious violation[11]. Finally, CEMBMD in Article 21 requires, in the most general way, a sanction by the Committee for Medical Ethics and Deontology of the Chamber, which must "file a complaint with the Prosecutor of the Chamber against members who violate one of the fundamental principles or certain provisions of the Code…"[12]. AHS defines minor and more severe service violations, such as causing harm to the health of patients by means of improper handling due to negligence or ignorance, disruption of profession's or employer's reputation, revealing professional secret... Disciplinary measures for minor and more severe service violations are determined by the Croatian Chamber of Healthcare Workers in its internal acts. Criminal regulations define fines for law breakers[13]. The Ethics and Deontology Commission of a particular vocational grade of the Croatian Chamber of Healthcare Workers is in charge of the established disciplinary breach and it issues a warning about the violation of the Code, the Statute, and other statutory acts of the Chamber. In the event of repeated offenses or in the case of a serious disciplinary offense, the proceedings shall be forwarded to the Courts of the Chamber. According to the Rulebook on Rights and Responsibilities, a warning, reprimand/public reprimand, fine, temporary/permanent seizure of work license is issued to a member of the Chamber[14].			

situations where consent would be impossible or impracticable to obtain, such as in retrospective-prospective research (e.g., use of existing samples on which it is proposed to implement a new analysis), it might be done only after consideration and approval of the local ethics committee[9,10,12].

It should be noted that the Code of Ethics, as the fundamental document of the professional law of medical biochemists, protects the profession and the individual very elegantly with the following formulation of Article 22 in an attempt to prevent confusion in practice: "If a medical biochemist is not sure whether a certain situation is in accordance with this Code, he/she shall consult with the Board of Medical Ethics and the deontology of the Medical Chamber"[12]. A proposal to define a laboratory protocol of conducting an 'informed consent interview' is shown in Table 2.

Conclusion

As initially stated, the clinical reality is constantly changing, so let us take a glimpse into the future of informed consent in laboratory practice. In the United States, a revision was conducted in 2011 with the aim to enhance the Federal Policy for the Protection of Human Subjects or the Common Rule. In 2015, a Notice of Proposed Rule Making was issued in the Federal Register and nearly 2200 public comments were received. They reveal differing opinions about the changes proposed. Final revisions to the Common Rule were issued by the U.S. Department of Health and Human Services (HHS) and fifteen other Federal Departments and Agencies in January 2017. The purpose was to implement better human research subject protection, but also to help (re)build public trust. The majority of changes will go into effect in January 2018[21-25]. Some of the major changes being proposed are those relating to informed consent, such as new consent elements, changes to waiver criteria and documentation, and a 'broad consent' (i.e. consent for future) option for unspecified future use of identifiable data/bisopecimens[26-28].

In the revised Common Rule, broad consent is defined as "seeking prospective consent to unspecified research"[26]. It represents an optional/alternative consent process for the storage, maintenance, and secondary usage of identifiable biospecimens for future, still unspecified research. Before 'activating' the obtained broad consent, the researcher should identify the types

Table 2. Proposal of a laboratory implementation protocol of an 'informed consent interview'

Elements of "informed consent interview"	Medical procedure		Research
	Patient/surrogate (with referral)	Patient/surrogate (without referral)	
Threshold elements (preconditions) 1. Competence (to understand and decide) check 2. Voluntariness (in deciding) check	 NO NO	 YES YES	 YES YES
Information elements 3. Disclosure (of medical information) 4. Recommendation (of a plan) 5. Understanding (of 3 and 4) check	 YES on patient's demand YES on patient's demand YES if 3 and 4	 YES YES YES	 YES YES YES
Consent elements 6. Decision (consent/refusal) 7. Authorization (i.e. signature)	 NO NO	 YES YES (in writing/ combined) *Exception: emergencies*	 YES YES (only in writing!) *Exception: when impossible to obtain consent*
Activation of Clinical Ethics Support System	Not needed	If dilemma occurs, contact the Medical Biochemists Chamber's Ethics Committee!	When impossible to obtain consent, research approval from local ethics committee is needed!

of research that may be conducted with the data/biospecimens, and determine whether proposed future secondary biospecimen use falls within the scope of the identified types of research[26-28].

The latter recommendation, should it be considered and adopted in Croatian laboratories, would greatly facilitate the implementation of studies on human material, as much as it may seem complicated at first glance to seek broad consent[27]. In any case, either through classical informed consent interview and/or approval by a local ethics committee (when needed), or by seeking broad consent, this would resolve one of the key issues encountered in everyday laboratory practice: should the rest of the blood remaining in the test tube after the completion of the required analysis be disposed of or can it be reused?

References

1. Nuremberg Code. In: Post SG, ed. Encyclopedia of Bioethics. 3rd edn. New York: Macmillan Reference USA, 2004; p. 2817-8.
2. Veatch RM. Abandoning informed consent. In: Kuhse H, Singer P, eds. Bioethics – An Anthology. Malden, Massachusetts: Blackwell Publishers, 1999; p. 523-32.
3. Turković K. [Pravo na odbijanje medicinskog tretmana u Republici Hrvatskoj]. Medicina. 2008;44:158-70. (in Croatian)
4. Faden RR, Beauchamp TL. History of informed consent. In: Post SG, ed. Encyclopedia of Bioethics. 3rd edn. New York: Macmillan Reference USA, 2004; p. 1271-7.
5. Beauchamp TL, Childress JF. Principles of Biomedical Ethics. 5th edn. New York: Oxford University Press, 2001; p. 57-112.
6. Šegota I. [Bioetički svesci br. 21: Informed Consent u Europi]. Rijeka: Department of Humanities, School of Medicine, University of Rijeka, 2001. (in Croatian)
7. Šegota I. [Rođenje i razvoj bioetike kao nove medicinske etike]. In: Šegota I. [Nova medicinska etika (bioetika)]. Rijeka: School of Medicine, University of Rijeka, 1994; p. 7-61. (in Croatian)
8. Universal Declaration on Bioethics and Human Rights. Available at: http://portal.unesco.org/en/ev.php-URL_ID=31058&URL_DO=DO_TOPIC&URL_SECTION=201.html, Accessed July 10, 2017
9. WMA Declaration of Helsinki. Available at: https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/ Accessed July 5, 2017
10. [Zakon o zaštiti prava pacijenata]. Available at: https://www.zakon.hr/z/255/Zakon-o-zaštiti-prava-pacijenata Accessed July 5, 2017 (in Croatian)
11. [Zakon o medicinsko-biokemijskoj djelatnosti]. Available at: http://www.zakon.hr/z/408/Zakon-o-medicinsko-biokemijskoj-djelatnosti, Accessed July 5, 2017 (in Croatian)

12. [Etički kodeks medicinskih biokemičara i medicinske deontologije]. Available at: http://www.hkmb.hr/dokumenti/propisi/kodeks.htm, Accessed July 5, 2017 (in Croatian)
13. Zakon o djelatnostima u zdravstvu. Available at: https://www.zakon.hr/z/442/Zakon-o-djelatnostima-u-zdravstvu, Accessed September 5, 2017 (in Croatian)
14. Pročišćeni tekst Kodeksa etike i deontologije djelatnosti sanitarnog inženjerstva, zdravstvene radiološko-tehnološke djelatnosti, djelatnosti radne terapije i medicinsko-laboratorijske djelatnosti. Available at: http://hkzr.hr/hr/wp-content/uploads/2011/10/Kodeks-etike-i-deontologije-djelatnosti-sanitarnog-in%C5%BEenjerstva-zdravstvene-radiolo%C5%A1ko-tehnolo%C5%A1ke-djelatnosti-djelatnosti-radne-terapije-i-medicinsko-laboratorijske-djelatnosti1.pdf, Accessed September 5, 2017 (in Croatian)
15. [Izjava – Kodeks etike i deontologije]. Available at: http://www.hkmb.hr/dokumenta/obrasci/, Accessed August 7, 2017 (in Croatian)
16. Dulčić K, Bodiroga-Vukobrat N. [Zaštita osobnih podataka pacijenata u europskom i hrvatskom pravu]. Zb Prav fak Sveuč Rij. 2008;29(1):371-411. (in Croatian)
17. Turković K. [Informirani pristanak]. Available at: http://www.hdgo.hr/userfiles/upload/documents/smjernice/zastita-pacijenata/Informirani-pristanak.pps, Accessed October 5, 2017 (in Croatian)
18. Nutbeam D. Health literacy as public health goal: a challenge for contemporary health education and communication strategies into the 21st century. Health Promot Int. 2000;15(3): 259-67. DOI: 10.1093/heapro/15.3.259
19. [Genetičko savjetovanje – stajalište Hrvatskog društva za humanu genetiku Hrvatskog liječničkog zbora]. Available at: http://www.humana-genetika.org/wp-content/uploads/2010/06/GENETSKO_SAVJETOVANJE-stajaliste_HDHG.pdf, Accessed October 6, 2017 (in Croatian)
20. Tests by Classification Type. New York State (NYS) Informed Consent Test List. Available at: https://www.mayomedicallaboratories.com/test-catalog/appendix/nys-informed-consent.html, Accessed August 5, 2017
21. Federal Policy for the Protection of Human Subjects ('Common Rule'). Available at: https://www.hhs.gov/ohrp/regulations-and-policy/regulations/common-rule/index.html
22. NPRM for Revision to Common Rule. HHS Announces Proposal to Improve Rules Protecting Human Research Subjects. Available at: https://www.hhs.gov/ohrp/regulations-and-policy/regulations/anprm-for-revision-to-common-rule/index.html, Accessed December 5, 2017
23. Notice of Proposed Rulemaking. Federal Policy for the Protection of Human Subjects. Federal Register 2015;80(173):53933-4061. Available at: https://www.gpo.gov/fdsys/pkg/FR-2015-09-08/pdf/2015-21756.pdf, Accessed December 5, 2017
24. Final Revisions to the Common Rule. Available at: https://www.hhs.gov/ohrp/regulations-and-policy/regulations/finalized-revisions-common-rule/index.html, Accessed December 5, 2017
25. Menikoff J, Kaneshiro J, Pritchard I. The Common Rule, Updated. N Engl J Med. 2017;376:613-5. DOI: 10.1056/NEJMp1700736
26. Revised Common Rule. Federal Register 2017:82(12):7149-7274. Available at: https://www.gpo.gov/fdsys/pkg/FR-2017-01-19/pdf/2017-01058.pdf, Accessed December 5, 2017
27. Attachment C – Recommendations for Broad Consent Guidance. Available at: https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-c-august-2-2017/index.html, Accessed December 5, 2017
28. U-M Implementation: Informed Consent Changes. Available at: http://research-compliance.umich.edu/human-subjects/common-rule-other-changes/u-m-implementation-informed-consent-changes, Accessed December 5, 2017

Sažetak

INFORMIRANI PRISTANAK U HRVATSKOJ KLINIČKOJ LABORATORIJSKOJ PRAKSI – AKTUALNA PITANJA I BUDUĆE PERSPEKTIVE

I. Sorta-Bilajac Turina i *V. Šupak Smolčić*

Rad se bavi mjestom i ulogom informiranog pristanka u svakodnevnoj kliničkoj laboratorijskoj praksi. Uzimajući u obzir međunarodne etičke smjernice kao što su UNESCO-va Opća deklaracija o bioetici i ljudskim pravima, Helsinška deklaracija Svjetskog medicinskog udruženja te hrvatske nacionalne zakone i kodekse kao što su Zakon o zaštiti prava pacijenata, Zakon o medicinsko-biokemijskoj djelatnosti, Etički kodeks medicinskih biokemičara i medicinske deontologije, Zakon o djelatnostima u zdravstvu te Etički kodeks Hrvatske komore zdravstvenih radnika daje se pregled aktualne primjene navedenih preporuka i propisa. Naglašava se potreba za razlikovanjem pristanka na medicinski postupak od pristanka na sudjelovanje u istraživanju. Ističe se uloga specijalista laboratorijske medicine i magistara medicinske biokemije u procesu informiranog pristanka. Sugerira se kreiranje 'intervjua informiranog pristanka'. Potrebna je daljnja rasprava o mogućnosti uvođenja 'opće suglasnosti'. Zaključno, informirani pristanak trebao bi predstavljati značajnu i uobičajenu aktivnost u kliničkim laboratorijima u Hrvatskoj.

Ključne riječi: *Obavješteni pristanak; Biokemija; Kliničke laboratorijske službe; Hrvatska*