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EDITORIAL

Dear Readers,

A new stage has come in the life of our journal. Since 2014, "Kutafin Law Review (KuLawR)" (until 2021 — "Kutafin University Law Review (KuLawR)") has been published regularly with a frequency of two issues per year. A distinctive feature of the journal was the focus on the publication of papers on individual problems of modern law. The journal gradually developed its circle of readers and authors, but contributions made gave reason to believe that the journal should change and develop.

The name of journal also reflects these changes. Since 2021, it has been changed for "Kutafin Law Review", although its acronym has been retained (KuLawR). This means that, on the one hand, the journal positions itself as an independent member among the Russian and international scientific periodicals, and on the other, it retains its spiritual and intellectual connection with the Oleg E. Kutafin scientific tradition, as well as with the university named after him.

The change in the format of the publication, the periodicity of new issues publication, as well as the editorial policy is designed to correspond to the latest trends in the development of both the world and domestic scientific periodicals.

The journal is published 4 times a year. With the doubling of the number of issues, while maintaining the previous volume standards, the principles of their content are changing, namely each issue will be devoted to a selected topic. The first issue offered to the reader is devoted to theoretical and applied problems of legal regulation of genetic research and biolaw; the nearest issues are to cover such topics as artificial intelligence and legal environment, legal issues of international scientific and technological cooperation, latest approaches in legal and forensic linguistics, legal didactics. The updated format of KuLawR assumes not only the preservation of its legal specialization, but also the strengthening of interdisciplinarity, suggesting the possibility of bringing topical issues to the pages of the journal, those of concern to the Russian and international community.

In each issue the journal seeks to present original scientific articles in which an author or a group of authors outlines the results of their research that constitutes an overview of the state legal knowledge in a particular area of law or some socially relevant law issues. The journal is published in English, but articles prepared in other language, for example in Russian or German, can be presented as two texts: the main one is given in English and additional — in the original language. In this case, both versions of the article will be published under a single title and with the same output data (DOI, issue number, and even page numbers).

In order to popularize domestic legal thought, the journal could present commentated translations of works of prominent Russian and Soviet legal scholars of the 19th–20th centuries, as well as articles and monographs of the last two decades, which present the latest achievements of Russian legal science. The journal publishes scientific reviews on published books, materials of scientific seminars and conferences, other texts covering the development of jurisprudence and social studies.

Vladimir I. Przhilenskiy,
Chief Editor

The presented issue of the journal opens a new era in its development.

This is the first of the so-called thematic issues of the journal. The first issue of KuLawR 2021 is devoted to an important cross-sectoral problem of legal regulation of genomic research and the use of genetic technologies.

Representatives of different scientific schools from different parts of our globe took part in the preparation of the issue.

I would like to express special gratitude to our foreign authors who found the time and opportunity to join an impromptu round table on such a topical topic of scientific research.

Three key issues were in the focus of the journal's authors: bioethics, medical law and the problem of international cooperation in the field of legal regulation of genomic research and the use of genetic technologies.

I am the first sailboat launched in the new era of the journal's development and we hope that the flotilla of such thematic issues will only be replenished with new issues and fresh ideas from their authors.

Maria V. Zhakarova,
Issue Co-Editor

RESEARCH ARTICLES

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Genetic Research Application in the Study of Pharmaceuticals

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Abstract: The current science and research trends, as well as the development of personalized medicine, point to the need to use genetic tests in course of the study of pharmaceuticals. Pharmacogenetic testing has become indispensable when developing new pharmaceuticals in order to study both the peculiarities of pharmacodynamic effects or the prospects of personalized treatment, and the characteristics of metabolism or drug-drug interaction. In addition, the introduction of pharmacogenetics in bioequivalence studies allows limiting, at early stages, the criteria for inclusion or non-inclusion of volunteers based on certain gene polymorphisms determining the metabolic rate.

The study of the genetic characteristics of clinical trial participants allows a more detailed analysis of the role of gene polymorphisms in terms of both pharmacokinetics and pharmacodynamics of the studied pharmaceuticals.

A separate important issue is genetic material collection from the clinical trial participants. On the one hand, the use of biological material collections is an essential tool for accomplishing the practical tasks in both the pharmaceutical industry and the state-of-the-art medicine. On the other hand, the legal review and ethics review of genetic material collection and use can become formidable barriers to the development

of biobanking. The existing legislative differences between Russia and other countries allow identifying the most challenging regulatory aspects, and can contribute to international law harmonization in the sphere of biobanking in the future.

Keywords: pharmacogenetics, biobanking, clinical studies, clinical trials, ethics review, law, legislation, genetic material

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Contents

I. Background

The current science and research trends, as well as the development of personalized medicine, point to the need to use genetic tests in course of the study of pharmaceuticals. Pharmacogenetic testing has become absolutely indispensable when developing new pharmaceuticals in order to study both the peculiarities of pharmacodynamic effects or the prospects of personalized treatment, and the peculiarities of metabolism or drug-drug interaction. In addition, the introduction of

pharmacogenetics in bioequivalence studies allows limiting, at early stages, the criteria for inclusion or non-inclusion of volunteers based on certain gene polymorphisms determining the metabolic rate. However, genetic material circulation in clinical studies/trials remains a subject of heated debate, both ethically and legally.

II. Pharmacogenetics in clinical studies

One of the key ways of improving the efficacy and safety of pharmacotherapy is the introduction of personalized (personified) medicine into the clinical practice. It is based on an individual approach to the choice of pharmaceuticals/drugs and the dosage regimen taking into account the factors influencing the pharmacological response of a particular patient (Kukes and Bochkov, 2007).

Currently, there are various points of view on the need for pharmacogenetic testing in clinical studies. Pharmacogenetic testing has become absolutely indispensable when developing new pharmaceuticals in order to study both the peculiarities of pharmacodynamic effects or the prospects of personalized treatment, and the peculiarities of metabolism or drug-drug interaction. The introduction of pharmacogenetics in bioequivalence studies allows limiting, at early stages, the criteria for inclusion or non-inclusion of volunteers based on certain gene polymorphisms determining the metabolic rate. This approach may reduce the number of study/trial participants. However, in crossover design conditions, the same subjects take part in both phases of the study (of the tested and the reference pharmaceutical), and their pharmacogenetic peculiarities do not change in these phases, and, therefore, the individual features have little effect on bioequivalence results. In this connection, the pharmacogenetic approaches to clinical studies/trials require special consideration, as they are directly related to the peculiarities of pharmacokinetics and the results of bioanalysis.

Interindividual differences in the pharmacological response can be explained by various factors: gender, age, bad habits, the functional state of organs and systems (primarily the gastrointestinal tract (GIT), liver, kidneys, and blood), the state and the etiology of the underlying disease, concomitant therapy, as well as the patient's genetic peculiarities, etc.

More often than not, the cause of undesirable (adverse) reactions of a human body to pharmaceuticals lies in the genetic characteristics (Karpenko, 2007). The study of the patients' genetic characteristics (peculiarities) formed the foundation for the development of pharmacogenetics and, later, personalized medicine.

All the stages of drug pharmacokinetics (absorption, distribution, metabolism/biotransformation, excretion) are regulated accordingly, therefore the polymorphisms of various genes can influence all of the aforementioned pharmacokinetic processes.

Identification of the patients' genetic characteristics (peculiarities) allows forecasting the pharmacological response to a drug/pharmaceutical, and, thus, increasing the efficacy and safety of its application, since the identification of the corresponding allelic variant leading to changes in the patient's pharmacokinetics and/or pharmacodynamics requires correction of the therapy (the dose of the pharmaceutical, as well as the frequency and the route of administration, or the need to replace it with another pharmaceutical). In other words, the use of this approach in clinical practice allows optimizing pharmacotherapy (Khokhlov et al, 2017).

Currently, the highest clinical importance is attributed to the gene polymorphisms which control the synthesis and the operation of the enzymes involved in biotransformation of pharmaceuticals, as well as transport proteins (transporters) involved in the processes of absorption, distribution and excretion of pharmaceuticals. For example, genetic polymorphism is characteristic of the genes encoding the enzymes for phase I metabolism, mainly Cytochrome P450 isozymes, and of the transporters, mainly P-glycoprotein (Avdeev, 2010).

The introduction of a personalized approach to treatment of various internal organ diseases into the medical practice is aimed at increasing both the efficacy of treatment and the safety of pharmacotherapy (Khokhlov, 2012). This is of special importance for a broad range of pharmaceuticals, such as anticoagulants, psychotropic medications, proton-pump inhibitors, as well as some pharmaceuticals for treatment of cardiac ischemia and hypertension (Morozova, 2016).

It is known that about 60 % of drug oxidization involves CYP3A4 enzyme system. CYP3A4 system, being the basic one in the human body,

is characterized by individual activity, and also by unimodal distribution in the population and absence of genetic polymorphism (Borodulin, 2011).

Interindividual differences in the rate of drug metabolism allow identifying groups of patients with different types of activity of certain isoenzymes.

"Extensive" metabolizers (extensive metabolism, EM) are individuals with a "normal" rate of metabolism of certain drugs, as a rule, homozygous for the "wild-type" allele of the corresponding enzyme gene. The majority of people are extensive metabolizers.

"Poor" metabolizers (poor metabolism, PM) are individuals with a low rate of metabolism of certain drugs, as a rule, homozygous (in case of autosomal recessive inheritance) or heterozygous (in case of autosomal dominant inheritance) for the "slow" allele of the corresponding enzyme gene. The characteristic feature of such patients is synthesis of a "deficient enzyme", or a total absence metabolic enzyme synthesis, which results in a decreased, or even zero, enzyme activity. Pharmaceuticals accumulate in high concentrations in the bodies of poor metabolizers, resulting in pronounced ADRs. Therefore, the drugs for poor metabolizers need to be dosed very carefully: the dose should be lower than that for extensive metabolizers.

"Ultra extensive" or "ultra rapid" metabolizers (ultra extensive metabolism, UM) are individuals with a high rate of metabolism of certain drugs, as a rule, homozygous (in case of autosomal recessive inheritance) or heterozygous (in case of autosomal dominant inheritance) for the "rapid/fast" allele of the corresponding enzyme gene. As a consequence, drug concentration in blood turns out to be insufficient to achieve a therapeutic effect. Therefore, the drug dose for ultra extensive metabolizers should be higher than for extensive metabolizers (Sychev et al., 2011).

In addition to cytochrome P450 isoenzymes, an important role in drug pharmacokinetics is played by P-glycoprotein, MRP, OATP, OST, and MATE. In the intestinal epithelium, P-glycoprotein provides the efflux of medication/drug (its substrate) into the intestinal lumen, thereby reducing the absorption thereof. In hepatocytes and renal epithelium, it mediates excretion of xenobiotics into the lumens of bile capillaries and renal tubules, respectively, and also provides impermeability of histohematogenous barriers to lipophilic substances (Ernest and Bello-

Reuss, 1998). Currently, the most studied polymorphism is the one associated with a change in the functioning of P-glycoprotein: it is a "silent" (i.e., not resulting in amino acid substitution) single-nucleotide substitution in exon 26 at position 3435 (C3435T), cytosine nucleotide substitution for thymine nucleotide in the promoter region of ABCB1 gene (formerly called MDR1), the gene encoding the P-glycoprotein synthesis (Yakusheva, 2011). It has been proved that, in homozygotes for the CC allele, the ABCB1 gene expression in the small intestine was more than twice higher than the expression in homozygotes for the TT allele, which indicated a higher activity of P-glycoprotein in CC genotype individuals. This is another proof of the need to study the ABCB1 genetic polymorphism with the purpose of pharmacotherapy individualization.

P-glycoprotein performs many various functions. The available data show that this protein functions as a body protector minimizing gastrointestinal absorption of xenobiotics and toxins, and stimulating the excretion thereof by the liver and kidneys (Andersen et al., 2009). It also takes part in aldosterone and cortisol secretion by the adrenal glands, and limits the penetration of glucocorticosteroids into the brain through the blood-brain barrier. Finally, it significantly contributes to the regulation of apoptosis, which is especially important in the treatment of malignant tumors, as one of the expected effects of chemotherapy is the activation of autogenous programmed death of mutated cells.

The biochemical compounds interacting with P-glycoprotein can be divided into P-glycoprotein substrates and P-glycoprotein inhibitors. The study of the ability of pharmaceuticals to suppress or enhance the P-glycoprotein function is of high practical importance, since these features can change the pharmacokinetics and bioavailability of pharmaceuticals when co-used, and lead to development of toxic effects of these pharmaceuticals, or, conversely, to a decrease in the concentration of substrates in blood and, as a consequence, to a decrease in their therapeutic activity (effect) (Collet et al., 2009).

Depending on various conditions, the same pharmaceuticals can act both as substrates and inhibitors for P-glycoprotein. For example, verapamil acts as a substrate of P-glycoprotein in small concentrations, but when the dose is increased, it exhibits the properties of an inhibitor of P-glycoprotein (Ramenskaya et al., 2007).

Bioequivalence studies are accumulating more and more data on the link (association) between polymorphisms of various genes and the individual pharmacokinetics, pharmacodynamics, efficacy, and safety of various pharmaceuticals. Thus, the pharmacogenetic testing results serve as a criterion for inclusion or non-inclusion of a volunteer into the study. But in that case, if it comes to registration of a pharmaceutical, the pharmacogenetic testing results will appear in the directions for drug use (medical application). A promising option is to use pharmacogenetic testing for biotransformation enzymes when selecting the volunteers for bioequivalence studies, which allows excluding "poor" or "ultra extensive" metabolizers, thereby reducing the coefficient of variation of pharmacokinetic parameters, and, hence, the number of volunteers required for participation, which might reduce the overall cost of the study (Sychev, 2016).

Since the emergence of the ideas about the genetic nature of pharmaceutical response variability, and over the next several decades, the system of clinical studies of pharmaceuticals and pharmacogenetics have evolved independently, without common points of contact. However, a number of recent research publications, as well as the development of the corresponding recommendations and guidelines, are evidencing the start of interaction. Perhaps, soon it will be impossible to perform a clinical study/trial (CT) without genetic information. The use of pharmacogenetic information in CTs can become widespread, since it does not require to develop a complex algorithm for interpreting the data generated during genetic testing. The point is that the objectives of personalized therapy differ from those of CTs: to predict the probability of side effects or the efficacy of treatment for a particular patient who is different from other individuals in many respects (e.g., in the predisposition to the development of certain side effects) is one thing, and to select CT participants with certain similar genetic features is quite another. However, after confirmation of the efficacy and safety of the studied pharmaceutical, the phase of larger-scale clinical trials with the involvement of a broader range of people begins. Here comes the question of whether the extent of the pharmaceutical activity (effect) will be the same, and whether it will be as safe for genetically diverse population of patients. To answer this question, additional studies/trials are required with the incorporation of

knowledge and experience of pharmacogenetics into CTs. Such studies do not necessarily generate an algorithm for taking into account genetic factors in doctor's prescriptions, but the very fact of such studies should ensure the safety of genetically diverse people. This means that the researchers should have a thorough understanding of metabolism and the action/effect of the studied pharmaceutical, and know what genetic factors may influence the pharmacological response (Khokhlov et al., 2017).

It is known that the genetics of model animals is of high importance at the preclinical trial stage. As a rule, genetically uniform inbred lines obtained through multiple mating of closely related specimen are used for that. Certainly, confirming the efficacy of a new pharmaceutical for humans during phase II CT with a limited number of volunteers is usually possible only with careful selection of the CT participants. Selection of the patients with a similar response [susceptibility] to the tested pharmaceutical it no less important than the "external" features (age, height, body mass index, etc.). Inclusion of genetic factors in the CT participant selection criteria will help to reduce the level of interindividual variability of the pharmacological response, making it possible to obtain more comprehensive information about drug effectiveness and safety using a small sample. For each drug/pharmaceutical, the "set" of identified genes will depend on the peculiarities of metabolism, the ways of excretion and the mechanism of action of the pharmaceutical, but the range of polymorphisms basically coincides with the list of genetic markers for which the evidence base was collected in course of pharmacogenetic studies. Among them, the polymorphism of the genes of cytochrome P450 isoenzymes, UDP-glucuronosyltransferases, N-acetyltransferase 2, some methyltransferases, drug transporters (P-glycoprotein, etc.) is of high importance. Attention should also be paid to the genes encoding the target molecules (receptors, enzymes, ion channels) of the pharmaceutical, and the proteins involved in certain pathological processes (blood clotting factors, apolipoproteins, HLA system genes, etc.) against which the tested pharmaceutical should act. State-of-the-art genetic testing is fast, reliable and valid for a lifetime. It is known that pharmacokinetic processes are more predictable than pharmacodynamic ones; therefore, pharmacogenetic tests allowing prediction of pharmacokinetics are used in clinical practice more often. First, it is easily determined and/or verified

by direct quantitative measurements. Second, the changes in enzyme activity, as a rule, affect several substrates in a similar way. Identification of the allelic variants well-known to researchers (e.g., CYP2C9*2, CYP2C9*3, CYP2C19*17, CYP2D6*4, etc.) can be used to study many substrates.

Genetic testing can also be supplemented with pharmacokinetic studies (e.g., phenotyping, which involves measuring the metabolic ratio in blood when administering the probe substrate). Study of genetic factors is practiced in many countries. In the US, the pharmacogenetic approach is regulated by the *Guidance for Industry: Clinical Pharmacogenomics: Premarket Evaluation in Early-Phase Clinical Studies and Recommendation for Labeling* (FDA), while the European Union has adopted such guidelines as *Reflection Paper on Pharmacogenomic Samples, Testing and Data Handling*, etc. *Guidance for Industry. E16 Biomarkers Related to Pharmaceutical or Biotechnology Product Development: Context, Structure, and Format of Qualification Submissions* has been published within the framework of conferences on harmonization (Khokhlov et al., 2017). In Russia *Recommendations for Pharmaceutical Companies on the Study of Biotransformation and Transporters of New Pharmaceuticals*, pointing out the need to take into account the genetic factors, were published in 2009 (Sychev, 2009). However, this is obviously insufficient for an active interaction between pharmacogenetic experience and clinical studies.

The US has broad experience in pharmacogenetic research and the use of the resulting information. The FDA Guidance mentions the following objectives for incorporation thereof in the CT process:

1. Identifying the basis for major individual deviations ("outliers") of pharmacokinetic processes and inter-subject variability in clinical response;

2. Excluding from clinical trials the participants with genetically induced deviations in the processes of pharmacokinetics and pharmacodynamics affecting the efficacy and safety of pharmaceuticals;

3. Estimating the magnitude of potential drug-drug interactions;

4. Investigating the molecular or mechanistic basis for the potential lack of efficacy or occurrence of adverse pharmaceutical reactions;

5. Designing clinical trials to test the effect of polymorphisms on the pharmacological response in certain subgroups (i.e., use in the population

"enrichment" strategy involving selection of the trial/study participants with a certain genotype).

The purpose of genetic testing in clinical studies/trials differs depending on the phase of the study of a new pharmaceutical. In the initial phase, participants with the most common genotype are selected (e.g., "poor" or "ultra extensive" metabolizers are not included). The final phases of clinical trials may include participants with significant genetically induced deviations in the pharmacological response.

In phases I and II of CTs, the following groups of participants are selected based on genetic features:

1. Groups of participants who should receive lower or higher doses of the studied pharmaceutical (which is usually due to the genetic differences in drug absorption, distribution, excretion, or metabolism). These trials/studies help to define the dose range for the subsequent CT phases;

2. Groups of participants who respond to therapy (this approach has become widespread in the oncologic setting);

3. Groups of participants with an increased risk of adverse drug reactions (the pharmaceuticals that cause such reactions are not acceptable if side effects cannot be predicted and/or prevented).

The EU guidelines also address a number of fundamental issues of genetic diagnostics applicability (Khokhlov et al., 2017).

It is assumed that pharmacogenetic studies assessing the pharmacokinetics of a new drug are necessary if the main metabolic pathways, or the transport of pharmacologically active drug compounds, and/or the active or toxic metabolites thereof, involve the proteins the activity of which depends on genetic polymorphisms. In order to plan the identification of genetic polymorphisms, a researcher should have a good understanding of the pharmacokinetic and pharmacodynamic processes in which the new pharmaceutical/drug is involved. When the molecular mechanisms are not known well enough, genetic approaches should be used in case of an unexplained variability in pharmacokinetic parameters. At the same time, it might become necessary to search for new pharmacogenetic factors. Gradually, as the cost of sequencing is decreasing, it is becoming possible to sequence polymorphic regions, which can be especially useful when searching for new significant polymorphisms. If unexplained changes in pharmacokinetics are detected, the samples of

the biological material containing the DNA are collected and stored for further work.

The EU documents specify that if a genotype predictably affects pharmacokinetics, efficacy and/or safety, genetic information should be involved at all CT phases. In this case, the extensive information collected can serve as a basis for development of pharmacogenetic recommendations. It is assumed that all the necessary pharmacogenetic information should be collected by the end of phase III CT. Based on the results of the trial/study, an assessment of the clinical consequences of genetic differences should be made using the statistical data.

In Russia, many international CTs are performed, including those involving collection of genetic material and pharmacogenetic testing. However, pharmacogenetic information analysis plays a secondary role, genotyping takes place on a voluntary basis, and the CT participants can refuse to take part in it while remaining included into the trial/study. In Russian CT practice, genetic information tends not to be taken into account in the initial phases, and pharmacogenetic studies usually take place in the later CT phases (which is still typical of the global practice as well).

In 2009, *Recommendations for Pharmaceutical Companies on the Study of Biotransformation and Transporters of New Pharmaceuticals: Research Design, Data Analysis and Information Entry into the Directions for Use* were published in Russia. As far as the use of genetic information is concerned, the *Recommendations* say only the following: "Identification of genetic polymorphisms of the enzymes involved in biotransformation is advisable for *in vivo* study participants when studying such cytochrome P450 isoenzymes as CYP2D6, CYP2C19, and CYP2C9" (Sokolov, 2015). The brochure *Evaluating the Bioequivalence of Pharmaceuticals — Methodology Guidelines*, that was issued around the same time, considers genotyping advisable if it is known that the studied pharmaceutical undergoes biotransformation controlled by genetically polymorphic cytochrome P450 isoenzymes (CYP2C9, CYP2C19, CYP2D6) in order to prevent participation of "poor" and "ultra extensive" metabolizers in the trial/study (the Scientific Centre for Expert Evaluation of Medicinal Products Federal Institution, 2008).

Both Russian documents (which are of a recommendatory nature) only point out the issue without any further details on the interaction between the pharmacogenetic and the clinical trials/studies. The strategies which can be applied in CTs based on genetic testing are not described either. However, the CTs based on pharmacogenetic testing are, undoubtedly, not only of scientific interest, but also of practical value. This can be illustrated by phase III of the multicenter clinical trial aimed at studying the efficacy of tiotropium bromide as an alternative to long-acting beta2-agonists for bronchial asthma patients homozygous for ADRB2 gene Arg/Arg16 (Cochran, 1963). This study was based on the concept that the replacement of one of amino acids (Argl6Gly) in the beta2-adrenergic receptor structure results in a more severe course of the disease, a decrease in the therapeutic response and acceleration of receptor desensitization when beta2-agonists are prescribed. That is why the use of M-anticholinergics can help to control the bronchial asthma symptoms for such patients. It has been demonstrated that tiotropium bromide, like salmeterol, significantly improves the lung function as compared to placebo when taken by patients with the genotype homozygous for ADRB2 gene Arg/Arg16 suffering from persistent bronchial asthma that cannot be controlled by inhaled glucocorticoids (Bateman, 2011).

Currently, high attention is paid to the clinical significance of such genetic characteristics of patients as polymorphism of SLC01B1 gene (encoding organic anion transporting polypeptides) in the development of myopathy when using statins, which is necessary to select the dosage regimen based on the pharmacogenetic testing results. Recently, the problem of statin safety — in particular, for the striated muscle tissue — has become increasingly relevant. While rhabdomyolysis, as a dangerous striated muscle complication resulting from the use of statins, is rare (0.15 per 1 million prescriptions), other forms of statin-induced myopathy in patients taking such kind of pharmaceuticals (Sychev, 2016) can occur frequently. In the SERCH study, 85 patients with statin-induced myopathy (90 patients without this complication made up the control group) demonstrated SLC01B 1*5 (c.521T>C) polymorphism as a genetic marker of this complication (Perez-Castrillon, 2010). Patients with the CC genotype taking 80 mg dose of simvastatin developed myopathy 17 times more often than patients with the TT genotype, and patients with the CT

genotype developed myopathy 2.5 times more often than patients with the TT genotype. Currently, the algorithms for personalizing statin use depending on the results of SLC01B1 pharmacogenetic testing (which has become possible for some commercial laboratories in Russia) have been developed.

Pharmacogenetic testing in bioequivalence studies was incorporated in the study of a group of NSAIDs, in particular lornoxicam. According to the results obtained, the presence of CYP2C9*2 and CYP2C9*3 alleles of cytochrome P450 gene in the volunteers' genotype demonstrated variations in the values apparently caused by differences in the volunteers' metabolism associated with the polymorphism of cytochrome P450 gene (CYP2C9). For instance, it was detected that the pharmacokinetics of lornoxicam largely depends on the CYP2C9 polymorphism leading to a significant increase in AUC and the drug half-life, as well as to a decrease in clearance in heterozygotes for cytochrome P450 isoenzyme gene as compared to homozygotes. It has been demonstrated that the occurrence of CYP2C9*2 and CYP2C9*3 alleles among the population of the Russian Federation is 18 %. Since the presence of CYP2C9*2 and CYP2C9*3 alleles (both in heterozygous and homozygous forms) significantly alters the metabolism of lornoxicam, it is considered appropriate to determine the cytochrome P450 gene polymorphism in people in order to reduce the variability of the pharmacokinetic parameters of lornoxicam (Khokhlov et al., 2017).

When conducting pharmacogenetic studies within the framework of CTs, different strategies are possible: the CT design based on genetic testing, the strategy of "enriching" the population of the CT participants, the design involving randomization of all subgroups (Matsui, 2013). The CT design based on genetic testing involves randomization of CT participants into two groups: in the first group, the treatment is adjusted based on genetic testing, while in the second group, the treatment is arranged regardless of the genetic factors. This approach allows assessing the influence of gene polymorphism on the clinical response, and concluding whether the pharmaceutical needs special recommendations taking into account the patient's genotype.

A very good result for a pharmaceutical is when there is no need to take into account the genetic factors during treatment, since the

pharmaceutical can be used irrespective of the patient's genetic status. If genetic factors strongly affect efficacy and safety, it may be necessary to include pharmacogenetic information into the directions for the pharmaceutical use. The strategy of "enriching" the population of the CT participants allows demonstrating the efficacy of a pharmaceutical in a relatively small group of patients by "shutting off" genetic diversity.

This approach can be applied almost throughout the entire CT, from phase I to phase III. First, predominantly homozygous wild-type carriers (the most common genotype) are selected. This is not always possible, but, in any case, the carriers of polymorphisms associated with the altered state of functioning of the protein products of the corresponding genes should be avoided. At later CT phases, the "enriching" strategy can be used to select, conversely, the CT participants with genetically determined deviations in the processes of pharmacokinetics and/or pharmacodynamics of the studied pharmaceutical (such samples allow determining the pharmaceutical dosage for certain individuals depending on their genotype).

The CT design involving the strategy of "enriching" the population of participants, includes the following stages:

1. Initial testing for planned genetic polymorphisms;

2. Only the participants with a certain specific genotype are admitted to take part in the CT;

3. Randomization of the participants admitted to take part in the CT based on the genotypes, and formation of the experimental group and the control group;

4. CTs in the experimental group.

Sometimes the information obtained as a result of pharmacogenetic study is used to "save" the pharmaceuticals that were previously rejected during the CT. For instance, in phase III CT of ximelagatran, an oral anticoagulant and a potent, competitive, reversible direct inhibitor of alpha-thrombin which causes the fibrinogen-fibrin conversion, hepatotoxicity manifestations of an immunological nature were detected. As a result, the pharmaceutical did not pass phase III CT and was not registered.

However, subsequent pharmacogenetic studies demonstrated that the hepatotoxicity of ximelagatran is connected with patients' genetic features, in particular, with the polymorphism of genes of one of the components

of the main histocompatibility complex. Therefore, the pharmaceutical may be used, but not for certain cohorts of patients (or the treatment of such cohorts of patients needs to be adjusted taking into account their individual genetic characteristics).

Thus, as the field of knowledge related to human genetic polymorphism expands, we sometimes get arrays of rather contradictory information, which is currently quite difficult to apply in practice (Khokhlov et al., 2017). There are relatively few algorithms for using pharmacogenetic knowledge in treatment, although their number is constantly increasing (March et al., 2001; Konstantinos, 2020). At the same time, the absence (or presence), in a pharmaceutical, of an obvious variability of the pharmacological response associated with genetic polymorphism is valuable knowledge in itself that must be established by the end of the CT. Pharmacogenetic testing allows, at the initial stages of clinical studies of bioequivalence, excluding from the experimental group the volunteers and/or patients significantly different in pharmacokinetic and pharmacodynamic parameters from the average statistical level of the target group, which, of course, means cost-effectiveness. In the later CT phases, conversely, it is possible to include into experimental groups the patients with genetically induced "deviations" of metabolic parameters, or transport of active components and/or active metabolites of the drug, or changes in the appropriate pharmacodynamic effect. CTs involving pharmacogenetic knowledge can have different designs, and allow expanding the understanding of efficacy and safety of the studied pharmaceutical, and, sometimes, adding the information obtained to the directions for drug use. Pharmacogenetics and CTs of pharmaceuticals can develop in close cooperation, mutually enriching each other (Khokhlov et al., 2017).

III. Biobanking

With the emergence of biobanking, a significant role in the development of state-of-the-art medicine and pharmaceutical industry is increasingly played by the use of collections of biological material for accomplishing research-related and practical tasks.

Comprehensive research directions, including fundamental and clinical research, educational programs, publications, etc., are related to the functioning and development of biobanks (Reznik et al., 2016).

Human biological material stored in biobanks, depending on the goals and needs of the end users, can be biopsy, blood, plasma, urine, fragments of DNA or RNA molecules, bone marrow, etc. The key tasks of biobanks are identification and validation of the diagnostic biomarkers necessary for adequate assessment of a developing pathology and prediction of the prospects thereof in a particular patient or person from the risk group, as well as establishment of links (associations) between the genes and diseases (the degree of associativity), selection of new pharmacotherapeutic targets (PTTs), and creation of innovative (mono- and multitarget) pharmaceuticals (Critchley et al., 2012).

There are several definitions of biobanking. Large international communities, such as the Organization for Economic Co-operation and Development (OECD), the International Society for Biological and Environmental Repositories (ISBER), the European Commission (EC) and the Biobanking and Biomolecular Resources Research Infrastructure (BBMRI) have their own definitions of this concept.

According to the OECD, a biobank is a collection of biological material, and the associated data and information stored in an organized system, for a population or a large subset of a population (The Organisation for Economic Co-operation and Development (OECD), 2006).

In the opinion of the International Society for Biological and Environmental Repositories (ISBER), a biobank is an entity that receives, stores, processes and/or distributes biospecimens, as needed (i.e., it encompasses the physical location of specimens, and the full range of activities associated with its operation) (Campbell, 2012).

The European Commission has its own point of view defining a biobank as an organized collection consisting of biological samples and related data that are of particular importance for fundamental science and the needs of personalized medicine (Zika et al., 2010).

According to one of the leading organizations in the sphere of biobanking at the moment — the Biobanking and Biomolecular Resources Research Infrastructure (BBMRI) — biobanks contain biological samples and the associated information that are the essential raw material for

the advancement of biotechnology, human health, and for research and development in life sciences (Assabler and Zatloukal, 2007).

Generalizing the concept of biobanking, one can refer to the widely accepted definition by Kauffmann and Cambon-Thomsen: a biobank is an organized collection of human biological material and associated information stored for one or more research purposes (Kauffmann and Cambon-Thomsen, 2008). At the same time, as genetic technologies develop, the potential goals and objectives of biobanks may expand. Definition of the range of possible, or permissible, objectives lies within the competence of policy makers and legislators. Therefore, approaches to biobanks, biobanking, or biobanking activities may vary (from liberal to conservative ones).

In general, a biobank can be described as a structure consisting of two parts: 1) the biological material that is collected, processed and stored for a long time; 2) the database with demographic and clinical data for each sample, enabling specimen collection, processing, storage, or inventory, and distribution of biological material (Artene et al., 2013).

It should be noted that the BBMRI classification currently distinguishes 2 types of biobanks (Holub et al., 2007; Yuille et al., 2007):

1) population biobanks (prospective biobanks focused on the study of various populations or certain social groups);

2) clinical biobanks (banks of tissue samples and clinical data intended for the study of diseases).

Studying the frequencies of clinically significant genetic polymorphisms in the population is a standard task for population biobanks. Such studies are key for Russia, since its population is characterized by an extremely high heterogeneity of the gene pool (Gorin et al., 2020).

In terms of the source of funding, the following biobank types are distinguished:

A) Public (state-run) biobanks (HUNT, Norway);

B) Private biobanks (deCODE, Iceland);

C) Public-private partnerships (UK Biobank).

At the same time, from the standpoint of sociologists and psychologists, the concept of “biobanking” includes the whole range of social, legal and ethical issues to be resolved as biobanks develop.

IV. Ethical issues of genetic material collection

The ethical and legal conflict associated with the activities of biobanks is due to the fact that the process of receipt, storage and use of biomaterial involves several participants. For example, donors are interested in ensuring privacy and information provision in order to control the use of biobank material (to introduce some ethical and/or other restrictions on access to the samples in connection with the donor's moral or religious views, changes in the donor's social or personal status, or the family's position, etc.)

Biobank owners are interested in autonomous use of material, and in independence from the donors, in order to expand the possibilities for using the results of their activities in science/research and for commercial purposes.

Scientists and researchers are interested in unrestricted and free-of-charge access to biobanks for work in sphere of pharmacogenetics, epidemiology, population studies, etc.

Any biobank is interested in people voluntary transferring their material and signing an informed consent form without strictly determining the purpose of the material use. This is due to the ethical issue arising with regard to biological material use. If a volunteer stipulates the conditions for the use of their genetic material (e.g., defines the scope/range of the experiments in which they are ready to take part), the biobank has to monitor the inclusion of the samples of that particular individual into the pool of the specimen and material for specific studies/trials. It becomes necessary to prevent inclusion of any biological material of that particular individual in some other experiments or further research. This creates organizational, technological and financial difficulties. Moreover, a volunteer, at the stage of publishing the research results (including the results obtained in course of their genetic information processing), may revoke/withdraw their consent for the genetic material transfer and for the use of the information obtained as a result of the genetic material analysis. If this happens, the use of the results becomes ethically illegitimate, and, therefore, the research becomes useless.

The key characteristic feature of international biobanks remains their "disconnection" (lack of integration) due to the absence of uniform legal norms, which significantly complicates the exchange of information between biobanks, and hinders efficient cooperation. Promising international projects are experiencing significant difficulties due to the non-uniformity of legal, ethical and other norms in different countries (Cailfield et al., 2014).

Currently, there exist a number of difficulties with international biobank creation: there are practically no legal norms or laws regulating the work with biological samples. The existing regulations are very different in different countries (Reznik et al., 2016).

The International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use proposed a harmonized trilateral ICH Guidance entitled *E15 Definitions for Genomic Biomarkers, Pharmacogenomics, Pharmacogenetics, Genomic Data and Sample Coding Categories* (dated 1 November 2007), and the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use developed harmonized ICH *E18 Guideline on Genomic Sampling and Management of Genomic Data* (dated 3 August 2017).

The main purpose of the aforementioned documents is to harmonize the principles of genomic sampling and genomic data management in clinical studies, as well as to increase awareness and provide a reminder regarding the need to respect the rights of participants in connection with the use of their personal information, protection of the data generated, the need to obtain informed consent, and the need to ensure transparency of findings in line with local legislation and regulations. Genomic research can be used at all stages or phases of pharmaceutical development. These documents are in full compliance with ethical requirements.

It is important to be able to integrate [combine] genetic/genomic data with other clinical data for use not only in current clinical studies, but also in the future. Therefore, it is recommended to store samples and data in the appropriate biobanks (Sayamov, 2020).

Key ethics-related concerns traditionally include informed consent, privacy (confidentiality) and data protection issues (Hawkins and O'Doherty, 2013).

According to the World Medical Association, the ethical principles for medical research apply to human subjects, including research on identifiable human material and data; and a physician shall act in the patient's best interest when providing medical care. This implies that collection, storage and use of samples of organs and tissues of a person is impossible without the consent of that person.

In accordance with international agreements and guidelines regarding research ethics (Fortier et al., 2011), informed consent must guarantee voluntary participation and describe the privacy issues. Informed consent consists of three main components: complete/ adequate information, voluntariness [confirmation that the consent is voluntary], and [legal] competence. This means that, before consenting, the biological material donor must clearly and fully understand their role in the study and the study purpose, be aware of the potential risks and side effects, and be able to refuse participation or withdraw from the study at any time. Informed consent is required when the study involves human beings, their genetic material, or personal data. Informed consent must protect the autonomy of an individual. Particular attention should be paid to certain groups of vulnerable people (such as children, elderly people, people with disabilities), and national background/peculiarities should also be taken into account.

There are heated debates around informed consent, and, in particular, its forms (whether it should be universal, or different for each new study taking into account the specifics). The main message is the use of two forms of informed consent in a clinical study. The first one is the "classic" ["traditional"] form providing the patient with the information about the clinical study, and containing all the sections and information required by the existing regulatory documents. The signing of this kind of form confirms the patient's consent and ability to participate in the given clinical study. The second one is the "genetic" form of informed consent. By signing it, the patient allows the use of their biomaterial for genetic research. At the same time, the patient's refusal to sign this kind of form does not limit their ability to participate in the clinical study as such.

Informed consent for the collection and use of genomic samples should permit extended analysis of the samples (e.g., gene set

identification, transcriptome analysis, or complete genome sequencing) regardless of the timing of the analysis.

The ethical principles regarding the information provided to patients are quite extensively described in Article 8 (paragraph *a*) of the *International Declaration on Human Genetic Data*, which says that prior, free, informed and express consent should be obtained for the collection of human genetic data, human proteomic data or biological samples, whether through invasive or non-invasive procedures, and for their subsequent processing, use and storage, whether carried out by public or private institutions. Informed consent is an extremely important document in clinical studies/trials not only because it can be withdrawn/revoked at any time, but also from the standpoint of privacy/confidentiality, or the possibility of using data for other research purposes for many years, etc.

The analysis of the clinical trial practice in Russia has demonstrated that almost all informed consent forms lack a section concerning the human right to decide whether or not to be informed about the results and consequences of the genetic analysis, as stipulated in the aforementioned document (Article 5, section *c*). However, this can be extremely important for the subsequent medical observation of the patient, for the selection of an appropriate occupation by the person (patient), for the patient's awareness of the undesirable/adverse effects of drug therapy associated with the peculiarities of genetically controlled metabolism, etc. (Sayamov, 2020).

Another important ethical issue of biobanking is confidentiality. Any biobank works with anonymized information about citizens. The problem of biobanking is how to reconcile the autonomous right of each person to manage their genetic material (including the right to determine what types of research are acceptable for that particular person) with the tasks of generating mass knowledge. This problem cannot be resolved using a standard algorithm for any biobank. Therefore, each biobank, depending on its purpose, the way of funding, and the scale of collections, always has to address the issues related to ethical and legal regulation.

On the other hand, there are proposals to create informed consent forms without any guarantees of anonymity, privacy and confidentiality

(Varkhotov et al., 2016). In the near future, the existing problems may be resolved through development of unified rules (protocols) and standards for working with biological specimen, i.e., the introduction of harmonization mechanisms allowing free exchange of biological specimen, and the information related thereto, following universal algorithms at the global level (Lunshof et al., 2008). The importance of harmonization is determined by the need to eliminate double interpretation of the same results by researchers in different countries through introducing strict standards for all biobanks (Reznik et al., 2016).

In recent years, hundreds of publications dealing with the link (association) between certain polymorphisms and the efficacy of pharmaceuticals for certain pathologies have appeared. Knowledge is being accumulated accompanied by creation of many databases and data banks including the results generated in course of clinical trials and treatment of diseases. Unfortunately, the protocols of IMCT (International Multicenter Clinical Trials), which are also performed in Russia, do not include any "feedback", and even the chief researchers of the studied pharmaceutical learn the genomic test results, including the possible associations with certain pathologies, after a long time and only from publications. Naturally, patients do not have this information either, which calls into question the ethics of such processes (Sayamov, 2020). This is important, since some genetic polymorphisms mean the need for changing the doses of the studied pharmaceuticals, or are significant for preventing undesirable side effects. Therefore, this information should be known not only to the doctor, but to the patient as well. However, there is almost never any feedback on the results of clinical studies involving pharmacogenetic testing with personal follow-up information provision to the patient.

Therefore, the current trends of genetic research expansion in the study of pharmaceuticals require further improvement of the regulatory framework.

V. Differences in the global and Russian practice of genetic material circulation

Currently, Russia is paying increasing attention to the development of science-intensive biomedical, genetic, and cellular technologies, which are impossible without developing biobanks. However, in terms of regulation, the issue of genetic material circulation in the Russian Federation is a complex problem obviously lacking appropriate legislative framework (Kosilkin, 2020).

While in Russia the authorities in charge of ethics reviews remain wary about permission to collect genetic material from clinical trial participants, in global practice the situation is the opposite. For example, Regulation (EU) (European Commission, 2017) encourages collection of biological samples for future research. In particular, *ICH E18 Guideline on genomic sampling and management of genomic data* (International Council for Harmonization, 2017) points out that the general approach of regulators in ICH regions is to encourage genomic research "which may or may not be pre-specified in the clinical study objectives at the time of collection" (E18 Section 1.2). In addition, it explicitly states that "genomic research could be used in all phases of drug development to assess genomic correlates of drug response, and to understand mechanisms of disease or drug pharmacology".

It also says that "Genomic research can be conducted during or after a clinical study. It may or may not be pre-specified in the clinical protocol" (E18 Section 1.3). The Guideline allows all kinds of work with the collected biomaterial within the scope of an informed consent (E18 Section 1.3), however, it recommends using a broad form of informed consent "permitting sharing and distribution" (E18 Section 4.2), and also permitting broad analysis of the samples "regardless of the timing of analysis. Ideally, informed consent should allow for broad use of the samples, such as assay development, disease research, drug response, or pharmacovigilance" (E18 Section 5).

At the same time, according to the Guideline, in some cases it is allowable not to communicate the results of future studies to the patients who provided the biomaterial (E18 Section 6), since the focus of the recommendation to collect biomaterial for future studies is not the

benefit of a particular patient, but a purely scientific goal of maximizing the value of the collected samples and the data generated from them (E18 Section 1.4). ICH E18 Guideline recommends collecting biomaterial at all phases and for all studies, if possible, from all participants (E18 Section 1.4): "With advances in science and increased awareness of the impact of genomics, there is a need and an opportunity to maximize the value of the collected samples and the data generated from them. Therefore, genomic sample acquisition is strongly encouraged in all phases and studies of clinical development. Moreover, the quality of genomic research is dependent upon unbiased systematic collection and analysis of samples, ideally from all subjects participating in the trial, in order to fully represent the study population" (International Council for Harmonization, 2017).

When a clinical trial participant gets the right to choose whether to permit the collection of their genetic material specified in the Patient Information Sheet within an informed consent form, they become able to independently make a decision about their readiness to make a specific contribution to science in the form of their biomaterial, which, as it accumulates in biobanks, will form the basis for the development of new pharmaceuticals and saving the lives of future generations.

At the same time, apart from the individual interests of researchers, as well as the interests of participants in clinical trials/studies, there exist some public and state (government) interests that do not always coincide. In addition to containing the information about a person and their genotype, the human genome allows obtaining (especially if a sufficiently large number of biosamples or relevant information about them is available) the data characterizing certain specific features, peculiarities, on the basis of which it is hypothetically possible to accomplish tasks aimed at solving both clinical and other problems.

For instance, in Israel, genetic data are successfully used to deal with the issue of belonging to a particular group, ethnicity. In Iceland, genetic information is used in order to avoid inbreeding.

The use of genetic technologies for purposes other than medical, and insufficient control over circulation of genetic information are beginning to pose a threat to citizens in labor relations and when dealing with certain types of insurance (first of all, voluntary health

insurance). The possibilities of discrimination against certain groups of people based on the probability theory, as well as the use thereof in actuarial calculations, are emerging.

The stored genetic information is also of interest to law enforcement authorities and courts, as it allows them to enhance the efficiency of handling their tasks.

A standalone problem is the emergence of biohacking and biocrime involving use of personal genetic information for criminal purposes (blackmail, bribery, disclosure of confidential information, etc.).

Besides, genetic information can be used in continuous attempts to develop biological and other selective-action weapons, as well as to determine the strategy and tactics of modern (including "hybrid") warfare.

The foregoing necessitates definition of a corridor of possibilities in this sphere, as well as differentiation of legal frameworks for circulation of certain types (units) of genetic information. This also brings about the issue of restrictions and prohibitions both in the sphere of genetic information circulation for accomplishing research-related and other tasks, as well as in related areas. For example, the choice of a biobanking model (liberal or conservative) is conditioned, on the one hand, by the originally formulated requirements for biological objects, biosamples of human origin, and, on the other hand, by understanding the technological possibilities of digitizing such objects (physical technical control is more difficult to ensure in this instance than for physical objects stored in biobanks).

In this connection, in addition to dispositive [discretionary] norms and contractual relations in this sphere, a set of imperative [peremptory] norms and requirements aimed at ensuring public interests in this area, will be formed.

Whereas the United States and some countries of Western Europe have "liberal" legislation in this sphere, the Asian countries — primarily China — stick to a "conservative" approach (which applies both to the sphere of biobanking and circulation of genetic information, and information in general).

It should also be noted that the major flow of biomaterials and information about biological objects goes into the US and some other

countries, but not out of them. In order to protect the US interests (including the sphere of information), special tools aimed at restricting the outflow of controlled materials, technologies, and information, can be actively applied. The US have a fairly developed legislation in the sphere of control over foreign economic activity in general, as well as technology transfer. At some points in time, Russia borrowed some of the legal means and mechanisms to protect its interests as well.

Some of the examples of such regulations are: Federal Law No 183-FZ [in Russian: 183-ФЗ] *On Export Control* dated 18 July 1999; Federal Law No 164-FZ [164-ФЗ] *On the Foundations of State Regulation of Foreign Trade Activities* dated 8 December 2003; Federal Law No 281-FZ [281-ФЗ] *On Special Economic Measures and Coercive Measures* dated 30 December 2006.

They do not directly mention the possibility of introducing (permanent or temporary) prohibitions or restrictions in relation to the issues under consideration, however, Russia can use some general or special legislative provisions with regard to foreign economic activities, if necessary.

For instance, a special economic measure under the Federal Law No 281-FZ *On Special Economic Measures and Coercive Measures* dated 30 December 2006 is the prohibition or refusal to participate in international research or research-and-engineering programs and projects of a foreign country.

Opportunities that have emerged in connection with the development of synthetic biology are becoming a standalone problem for legislators requiring a detailed study in order to develop sound recommendations. Whereas before its advent the efforts of researchers were focused on isolating, studying, digitizing a biological object, as well as storing the object itself and (or) the information about it, the development of synthetic biology has brought about a hypothetical opportunity — drawing on information and existing technologies (genome editing, bioprinting, cloning, etc.) — to reproduce a biological object only on the basis of information about it or create a new biological object, a living system. Therefore, the availability of information and technologies changes the paradigm of many processes, both opening up

new opportunities and bringing about new risks and threats for people, society, and the state.

Based on the above, the definition of the basic model of circulation of biomaterial, genetic material, as well as biological and genetic information, needs to take into account the entire range of private, public, and state interests.

VI. Conclusion

The aspects of genetic material use in clinical studies/trials analyzed here allow highlighting the complex and controversial problems faced by both pharmaceutical manufacturers and regulatory authorities. The existing differences in the legislative regulation of genetic material circulation in different countries emphasize the high relevance of the issue and allow finding the ways to harmonize international and national law in the sphere of genetic information circulation in general, and in the sphere of biobanking, taking into account both private and public interests, traditions, and development priorities, as well as risks and threats in this area.

References

1. Andersen, V. et al., (2009). Polymorphisms in the xenobiotic transporter Multipharmaceutical Resistance 1 (MDR1) and interaction with meat intake in relation to risk of colorectal cancer in a Danish prospective case-cohort study. *BMC Cancer,* 9, p. 407.

2. Artene, S.A., Ciurea, M.E., Purcaru, S.O. et al., (2013). Biobanking in a constantly developing medical world. *The Scientific World Journal*, 343275, 1–4.

3. Assabler, M., Zatloukal, K., (2007). Biobanks: transnational, European and global network. *Brief. Funct. Genomic. Proteomic,* 6(3), pp. 193–201.

4. Avdeyev, R.M. et al., (2010). Genetic Polymorphism and Ethnic Aspects of Pharmacogenetics. *Medical Genetics*. 5(6), pp. 11–15. (In Russ.).

5. Bateman, E.D., Kommann, O., Schmidt P. et al., (2011). Tiotropimn is noninferior to salmeterol in maintaining improved lung function in

B16-Arg/Arg patients with astluna. *Journal of Allergy and Clinical Immunology*, 128(2), pp. 315–322.

6. Borodulin, V.D. et al., (2011). Association of Polymorphism of CYP2D6 and CYP2C9 Genes Encoding the Proteins of Cytochrome P-450 with the Degree of Arterial Hypertension. *Saratov Journal of Medical Science and Research*, 8(4), pp. 933–937. (In Russ.).

7. Cambon-Thomsen, A., Rial-Sebbag, E. and Knoppers, B.M., (2007). Trends in ethical and legal frameworks for the use of human biobanks. *The European Respiratory Journal*, 30(2), pp. 373–382.

8. Campbell, L.D. (ed.), (2012). *2012 Best Practices for Repositories Collection, Storage, Retrieval, and Distribution of Biological Materials for Research*. 3rd edn. International Society for Biological and Environmental Repositories. *Biopreservation and Biobanking*, 10(2), pp. 79–161, doi: 10.1089/bio.2012.1022. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24844904.

9. Caulfield, T., Burningham, S. and Joly, Y. et al., (2014). A Review of the Key Issues Associated with the Commercialization of Biobanks. *Journal of Law and Biosciences*, 1(1), pp. 94–110.

10. Chinn, L. and Kroetz, D., (2007). ABCB1 Pharmacogenetics: Progress, Pitfalls, and Promise. *Clinical Pharmacology & Therapeutics*, 81(2), pp. 265–269.

11. Cochran, W.G., (1963). *Sampling Techniques*. 2nd ed. New York: John Wiley and Sons, Inc.

12. Collet, J.P., Hulot, J.S., Pena, A. et al., (2009). Cytochrome P450 2C19 polymorphism in young patients treated with clopidogrel after myocardial infarction: A cohort study. *Lancet*, 373, pp. 309–317.

13. Critchley, C., Nicol, D., Otlowski, M. and Stranger, M., (2010). Predicting intention to biobank: a national survey. *The European Journal of Public Health*, 22(1), pp. 139–144.

14. Ernest, S. and Bello-Reuss, E., (1998). P-glycoprotein functions and substrates: possible roles of MDR1 gene in the kidney. *Kidney International Supplements*, 65, pp. 11–17. (In Russ.).

15. European Council. *Ethical considerations for clinical trials on medicinal products conducted with minors*. (2017). Recommendations of the expert group on clinical trials for the implementation of Regulation (EU) No 536/2014 on clinical trials on medicinal products for human

use. Available at: https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-10/2017_09_18_ethical_consid_ct_with_minors.pdf (Accessed 21 April 2021).

16. European Council. *Ethics for researchers. Facilitating research excellence in FP7.* (2013). Luxembourg: Publications Office of the European Union. Available at: https://ec.europa.eu/research/participants/data/ref/fp7/89888/ethics-for-researchers_en.pdf (Accessed 21 April 2021).

17. Fortier, I., Doiron, D., Burton, P. et al., (2011). Invited commentary: consolidating data harmonization — how to obtain quality and applicability. *American Journal of Epidemiology,* 174, pp. 261–264.

18. Gorin, I.O., Petrushenko, V.S., Zapisetskaya, Yu.S., Koshel', S.M. and Balanovskiy, O.P., (2020). Population Biobank Application for Analyzing the Frequencies of Clinically Significant DNA Markers in the Population of Russia: Bio-informational Aspects. *Cardiovascular Therapy and Prevention*, 19(6), pp. 27–32, doi:10.15829/1728-8800-2020-2732.

19. Hawkins, A.K. and O'Doherty, K.C., (2011). «Who owns your poop?» Insights regarding the intersection of human microbiome research and the ELSI aspects of biobanking and related studies. *BMC Medical Genomics*, 11(4), p. 72.

20. Holub, P., Swertz, M., Reihs, R., van Enckevort, D., Müller, H. and Litton J.E., (2016). BBMRI-ERIC Directory: 515 Biobanks with Over 60 Million Biological Samples. *Biopreserv Biobank,* 14(6), pp. 559–562.

21. Karpenko, M.A., (2007). *Arterial Hypertension: Age, Gender and Genetic Peculiarities. Doctoral Dissertation (Doctor of Medical Science).* Moscow. (In Russ.).

22. Kauffmann, F. and Cambon-Thomsen, A., (2008). Tracing biological collections: between books and clinical trials. *JAMA*, 299(19), pp. 2316–2318.

23. Khokhlov, A.L. et al., (2012). Importance of Determining the Polymorphisms of the Genes Responsible for the Activity of Angiotensin-Converting Enzyme in the Patients with Arterial Hypertension and Chronic Cardiac Insufficiency for Optimizing the Arterial Hypertension Treatment Standards. *Problems of Standardization in Healthcare,* 4, pp. 41–44. (In Russ.).

24. Khokhlov, A.L. et al., (2017). *Theoretical and Practical Foundations for Conducting Research of Generic Drugs: Monograph*. Moscow-Yaroslavl-Prague: Photolife Press. (In Russ.).

25. Khokhlov, A.L., Kukes, V.G. and Sychev, D.A., (2016). *Approaches to Pharmacogenetic Studies of the Diseases Associated with Lipid Metabolism Disorders and Atherosclerosis*. Moscow: Yaroslavl Press. (In Russ.).

26. Khokhlov, A.L., Pozdnyakov, N.O. and Rybachkova, Yu.V., (2016). *Importance of Pharmacogenetic Studies for Various Forms of Cardiac Ischemia*. Yaroslavl: Remder Press. (In Russ.).

27. Klaassen, C.D. et al., (2010). Xenobiotic, bile acid, and cholesterol transporters: function and regulation. *Pharmacological Reviews*, 62(l), pp. 1–96.

28. Konstantinos, G., (2020). Regulatory Aspects of Genomic Medicine and Pharmacogenomics, in Patrinos, G.P., (ed.) *Applied Genomics and Public Health*. Elsevier: Academic Press, pp. 345–360, doi:10.1016/b978-0-12-813695-9.00020-0.

29. Kosilkin, S.V., (2020). Experience of Legal Regulation of Biobank Activities in Global Practice and Development of Russian Legislation. *Courier of Kutafin Moscow State Law University (MSAL),* 4(68), pp. 79–87. (In Russ.).

30. Kukes, V.G., Bochkov, N.P., (2007). *Clinical Pharmacogenetics*. Moscow: Geotar-Media Press. (In Russ.).

31. Lunshof, J.E., Chadwick, R., Vorhaus, D.B. et al., (2008). From genetic privacy to open consent. *Nature Reviews Genetics*, 9(5), pp. 406–411.

32. March, R., Cheeseman, K., and Doherty, M., (2001). Pharmacogenetics — legal, ethical and regulatory considerations. *Pharmacogenomics,* 2(4), pp. 317–327, doi:10.1517/14622416.2.4.317.

33. Matsui, S., (2013). Genomic Biomarkers for Personalized Medicine: Development and Validation in Clinical Studies. *Computational and Mathematical Methods in Medicine*. Available at: https://pubmed.ncbi.nlm.nih.gov/23690882/.

34. Morozova, T.E. et al., (2016). Pharmacogenetic Approaches to Forecasting the Efficacy and Safety of Arterial Hypertension Pharmacotherapy. *Healthcare Practitioner*, 3, pp. 77–81. (In Russ.).

35. Ozawa, S., Soyama, A., Saeki, M., Fukushima-Uesaka, H., Itoda, M., Koyano, S., Sai, K., Ohno, Y., Saito, Y. and Sawada, J., (2004). Ethnic Differences in Genetic Polymorphisms of CYP2D6, CYP2C19, CYP3As and MDR1/ABCB1. *Drug Metabolism and Pharmacokinetics*, 19(2), pp. 83–95.

36. Perez-Castrillon, J.L., AbadManteca L., Vega G. et al., (2010). Vitamin D levels and lipid response to atorvastatin. *International Journal of Endocrinology*. Available at: https://pubmed.ncbi.nlm.nih.gov/20016682/ [Accessed 21 April 2021].

37. Ramenskaya, G.V., Faynshteyn, S.L. and Sychev, D.A., (2007). Importance of Change in the Functional Activity and the Amount of Expressed P-glycoprotein in Drug Pharmacokinetics. *Experimental and Clinical Pharmacology*, 70(1), pp. 72–80. (In Russ.).

38. Reznik, O.N., Kuz'min, D.O., Skvortsov, A.E. and Reznik A.O., (2016). Biobanks: an Invaluable Resource for Transplantation. History, Current State, Prospects. *Bulletin of Transplantology and Artificial Organs*, (4)XVIII, pp. 123–132. (In Russ.).

39. Sayamov, Yu.N., (2020). *Bioethics and the Global Challenges. Documents and Reflections*. Moscow: Veche publ. (In Russ.).

40. Scientific Centre for Expert Evaluation of Medicinal Products Federal Institution. *Methodology Guidelines of the Scientific Centre for Expert Evaluation of Medicinal Products Federal Institution*? (2012). Available at: http://rdg-cro.com/wp-content/uploads/2012/07/Guidelines-for-conducting-bioequivalence-studies-in-Russia.pdf [Accessed 21 April 2021].

41. Scientific Centre for Expert Evaluation of Medicinal Products Federal Institution. *Evaluation of Bioequivalence of Drugs*. (2008). Methodology Guidelines of the Scientific Centre for Expert Evaluation of Medicinal Products Federal Institution. Available at: http://rdg-cro.com/wp-content/uploads/2012/07/Guidelines-for-conducting-bioequivalence-studies-in-Russia.pdf [Accessed 21 April 2021].

42. Sokolov, A.V., Kukes, V.G., Bunyatyan, N.D. et al., (2015). Pharmacokinetic Approach to the Issue of Drug Interchangeability. *Biomedicine,* 3, pp. 43–51.

43. Sychev, D.A. (ed.), (2009). *Recommendations for Pharmaceutical Companies on the Study of Biotransformation and Transporters of New*

Pharmaceuticals: Research Design, Data Analysis and Information Entry into Directions for Use. Available at: http://www.regmed.ru/ Content/ Doc.aspx?id=26a9128c-ee32-4469-9c64-5c666339049e [Accessed 21 April 2021].

44. Sychev, D.A. et al., (2011). Pharmacogenetic Technologies of Personalized Medicine: Optimization of Drug Administration. *Terra Medica,* 1, pp. 4–9.

45. Sychev, D.A., (2016). Pharmacogenetic Testing in Clinical Trials. *Pharmacogenetics and Pharmacogenomics*, 1, p. 13. (In Russ.).

46. The International Council for Harmonisation. *ICH Harmonized Guidelines. ICH E18 Guideline on Genomic Sampling and Management of Genomic Data*. (2017). Available at: https://www.ema.europa.eu/en/ich-e18-guideline-genomic-sampling-management-genomic-data. [Accessed 21 April 2021].

47. The Organisation for Economic Co-operation and Development (OECD). *Creation and Governance of Human Genetic Research Databases. Glossary of Statistical Terms*. (2006). Available at: http://stats.oecd.org/glossary/detail.asp?ID=7220 [Accessed 1 Aug 2016].

48. Varkhotov, T.A., Gavrilenko, S.M., Stambol'skiy, D.V., Ogorodova, L.M., Bryzgalina, Ye.V. and Alasaniya, K.Yu., (2016). Objectives of Social and Humanitarian Support during Creation of a National Depository Bank for Biomaterials in Russia. *Issues of Philosophy*, 3, pp. 124–138. (In Russ.).

49. Yakusheva, E.N., Chernykh, I.V. and Biryukova, A.S., (2011). Characteristics of P-glycoprotein as a Medication Transporter. *Pavlov Russian Medicine and Biology Bulletin*, 3, pp. 142–148. (In Russ.).

50. Yuille, M., van Ommen, G.-J., Bréchot, C. et al., (2007). Biobanking for Europe. *Brief Bioinform*. 9 (1), pp. 14–24, doi: 10.1093/bib/bbm050.

51. Zika, E., Paci, D., Bäumen, S. et al., (2010). *Biobanks in Europe: prospects for harmonisation and networking. JRC Scientific and Technical Reports*. L.: Publications Office of the European Union. Available at: http://www.eurosfaire.prd.fr/7pc/doc/1280153287_biobanks_eu_jrc57831.pdf [Accessed 1 Aug 2016].

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Contemporary Challenges and Legal Regulation of Genome Research: Some Considerations

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***Abstract*:** The paper studies some aspects and considerations of the legal regulation of genomic research in the context of modern challenges. Approaches to the formulation of some basic concepts in the field of bioinformatics, such as information, information space, are proposed, the importance of these concepts for legal regulation is substantiated. Approaches to the legal regulation of the commercial use of the results of genomic research in the field of bioinformatics are formulated. Approaches to the legal regulation of the activities of biobanks are proposed based on the analysis of the possibility of using blockchain technology to improve the functioning of the biobank, the possibility of attracting investments through crowdfunding financing. The classification of biobanks according to various criteria is given. Approaches to the formulation of such concepts as donation and parenthood are determined within the framework of the legal regulation of genomic research in the field of human reproduction. The influence of modern challenges associated with the development of science and technology on the formulation of these concepts is considered. Approaches to solving the problem of ensuring a balance of private, group and general interests in the field of legal regulation of genomic research are proposed.

***Keywords*:** legal regulation, genomic research, bioinformatics, biobanks, blockchain, crowdfunding, donation, parenthood, balance of interests, information society, economic models, commercial use, human reproduction, comparative legal research

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Contents

I. Introduction

Within the framework of this paper, we would like to dwell on some aspects and considerations of the legal regulation of genomic research in the field of reproduction, biobanking and bioinformatics, which arose in connection with the emergence of new factors that significantly affect social relations, including those in such a sensitive area as genomic research.

In our opinion, one of the defining factors affecting social relations is the transition to an information society from an industrial society.

An information society is a society in which information and the level of its application and accessibility radically affect the economic and socio-cultural living conditions of citizens.

The information society is opposed to the industrial society, which was formed in the process and as a result of industrialization, the development of machine production, the emergence of adequate forms

of labor organization, the application of the achievements of technical and technological progress (Rayzberg, Lozovskiy and Starodubtseva, 2011).

According to the American sociologist D. Bell, the information society is a post-industrial society characterized by the transition from the production of things to the production of services, changes in the employment of the population and the central role of theoretical knowledge (Bell, 1999).

II. Bioinformatics: Basic Concepts and Approaches to the Commercial Use of Research Results

The rapid development of information technology has led to the emergence of new branches of knowledge and science, new areas of activity, areas of application of new technologies. With regard to the field of genomic research, we can talk about the emergence of such a branch of knowledge as bioinformatics.

Bioinformatics is a relatively new and rapidly developing discipline. As rightly noted by D.V. Ponomareva, genetic information and the way we use it are already changing our world, our views on human history and our approach to health matters (Ponomareva, 2020). All this makes bioinformatics an increasingly topical field of knowledge that requires legal research in order to form a regulatory environment.

Approaches to formulating the very concept of bioinformatics are quite different. So, for example, in the Russian Federation the definition of bioinformatics in one of the regulatory legal acts is formulated as follows: Bioinformatics (syn. — "Computational Biology") is a biological discipline engaged in the research, development and application of computational methods (including computer) and approaches to expand the use of biological, behavioral or health data.[1]

Foreign researchers, for example, give the following definitions of bioinformatics:

[1] "VP-P8-2322. Comprehensive program for the development of biotechnology in the Russian Federation for the period up to 2020" (approved by the Government of the Russian Federation dated 24.04.2012 No 1853p-P8).

The field of bioinformatics includes the storage, retrieval, and interpretation of various types of biological data, including nucleotide and amino acid sequences, protein domains, and protein structures. One of the main tasks of bioinformatics is the study and development of tools that provide effective access to and management of various biological data (Hamdi-Cherif, 2010).

Bioinformatics is the use of computers to handle, and interpret, biological information (McCubbin, 2003).

Bioinformatics: an umbrella term linking biological data with techniques for information storage, access, and analysis to support multiple areas of scientific research and clinical treatment (Capps et al., 2019).

As we can see, the definitions are very different. The main characteristic of bioinformatics, which is reflected at almost all definitions or concepts, is the connection between biological data and information, the processing of biological data using computer information technologies.

For the purpose of formulating approaches to the legal regulation of this sphere of social relations, in our opinion, it would be advisable to consider in more detail the concept of information and information space, which is even more relevant, given the development of an informational, post-industrial society.

The concept of information first became an object of deep scientific research with the advent of cybernetics. The founder of this science N. Wiener determined that information is not energy or matter, but a designation of the content received from the external world in the process of adaptation to it (Wiener, 1958). As you can see, the specified definition of information reflects two important features of this concept, which are recognized by most researchers of information as a phenomenon. First, it is established that the information is intangible. It is this feature that determines the specifics of the legal regulation of information relations. Secondly, N. Wiener's definition indicates that information is a certain content, that is, information, facts obtained from the external world in the process of adaptation, and, consequently, in the process of interaction with the external world.

A similar definition can be found in the dictionary of S.I. Ozhegov (1990). In accordance with this definition, information is 1) data about the surrounding world and the processes occurring in them, perceived by a person or a special device, 2) generalizations, informing about the state of affairs, about the state of something (Ozhegov, 1990).

Considering information from a socio-economic point of view, a number of domestic scientists have formulated the following definition: information is a set of data about nature and society, the processes that occur there and are reflected in the consciousness of people (Plakhotnoy, 1992).

In some cases, information is understood not as specific data, facts, but as a process of transmission of messages, data. For example, in the Soviet encyclopedic dictionary, information is the exchange of data between people, a person and an automaton, an automaton and an automaton, the exchange of signals in the plant and animal world, the transmission of signs from organism to organism (Soviet Encyclopedic Dictionary, 1989, p. 504).

According to Ermishina (1988), information is the transmission of news, messages about events, as well as scientific and technical information, videotapes and records, various types of printed information, etc. There is distinction between the concept of "information" as a means, process and "information" as a result. As you can see, in this definition she attempts to combine two main features in the concept of information: first, to present information as data, facts, and secondly, to consider information as a process of data transferring.

According to the Dictionary of Foreign Words, the concept of information includes: 1) a message about something, 2) information that is an object of storage, processing and transmission, 3) in mathematics, cybernetics — a quantitative measure of eliminating uncertainty (entropy), a measure of system organization (Modern Dictionary of Foreign Words. 1993, p. 254).

According to UNESCO, information is a universal substance that permeates all spheres of human activity, serving as a conductor of knowledge and opinions, an instrument of communication, mutual understanding and cooperation, and the approval of stereotypes of thinking and behavior (Lopatin, 2000).

A very important feature of information, which, on the one hand, determines the complexity of the legal regulation of social relations concerning information, the difficulty of establishing a legal regime, and on the other hand, determines the simplicity and ease of occurrence, change and termination of these relations, is the intangible nature of information. Nevertheless, information, being intangible in essence, cannot be considered without a tangible carrier, while it is necessary to distinguish between relations regarding information, information carrier and information located on the information carrier. This feature, which characterizes information as a combination of intangible content and material carrier, is of great importance for understanding the essence of the information space, approaches to legal regulation of which will be discussed later.

Thus, based on the generalization of the main features of information, the following definition of the concept of "information" can be proposed: Information is an intangible object that is data, facts, as well as the results of their assessment in the mind of a person, mediating interactions and connections within the framework of human society, systems subject-object, subject-subject, object-object, as well as a set of genetic characteristics of the organism. Information is also a process of transferring information, messages, facts, signs from organism to organism in living nature.

The development of information technology has led to the widespread penetration of the Internet both in everyday life and in scientific life. All this allows us to speak about the formation of the information space as a special sphere of social relations in connection with information, including directly related to bioinformatics.

Various definitions of information space or information environment are now known. For example, according to the UN Secretary General's Report, the information space is understood as the sphere of activity related to the creation, transformation and use of information, including individual and social consciousness, information and telecommunication infrastructure and own information.[2]

Within the framework of the CIS, the following definition of the information space was developed: information space — a set of

[2] UN document A/55/140, p. 3.

databases and data banks, information and telecommunication networks and systems, as well as technologies for their maintenance and use, functioning on the basis of general principles and according to the rules that ensure information interaction between organizations and citizens, and also meeting their information needs.[3]

In the Decree of the President of the Russian Federation dated 09.05.2017 No 203 "On the Strategy for the Development of the Information Society in the Russian Federation for 2017–2030", the information space is defined as a set of information resources created by subjects of the information sphere, interaction facilities of such subjects, their information systems and the necessary information infrastructure.[4]

Thus, the information space includes two components: the information itself and the information infrastructure. It seems that when defining an information space, we should proceed basing on the presence of two aspects in information relations. Consequently, the information space can be defined as a sphere of activity that includes information itself, relations regarding the production, collection, search, processing, storage and distribution of information, as well as information infrastructure, including computers and information and telecommunication networks.

The definition of the information space in relation to the legal regulation of relations in the field of bioinformatics is important due to the fact that these relations are largely global in nature, databases are interconnected using information technologies, access to databases under certain conditions can be obtained from anywhere by using the Internet, the software is also distributed using the Internet, etc.

As shown above, information itself is intangible, but at the same time, it cannot exist without a material carrier, which characterizes the substantial dualism of information. Accordingly, in any relationship with regard to information, including in the field of bioinformatics, it is necessary to distinguish between two main aspects: relations associated

[3] Decision of the CIS Economic Council "On the Concept of Scientific and Information Support of Programs and Projects of the CIS Member States in the Innovation Sphere" (Adopted in Moscow on 13.03.2009).

[4] Collection of Legislation of the Russian Federation, 2017, No 20, Art. 2901.

with information as an intangible substance, and relations associated with a material component (material carriers in a broad sense, objects of information infrastructure etc.).

Based on this, the approach to legal regulation can be different. Since relations regarding the material component are associated with the location and/or placing of relevant objects in certain territories that are related to a particular state and in which the state has sovereignty and, accordingly, the authority to establish legal regimes, in this part, harmonization of legislation and legal regulation in different states is possible. If we talk about the intangible component, then in this area, in our opinion, it is precisely international legal regulation or at least regulation at the level of regional integration formations is necessary, since the exchange of information may not be related to the state borders and sovereignty of any particular state.

Thus, we believe that the legal regulation of social relations in the field of bioinformatics should take into account the substantial dualism of information and, in this regard, may be a combination of international legal regulation and (or regulation at the level of regional integration entities) and harmonization of legislation and legal regulation of various states.

Within the framework of this article, we would also like to dwell on the formation of approaches to the legal regulation of the commercial use of the results of genomic research in the field of bioinformatics.

For this purpose, it seems necessary to outline the areas in which the commercial use of such results is possible.

According to some authors, Commercial value is realized in bioinformatics through the exploitation (often by way of license arrangements) of intellectual property rights in the biological molecules, databases and software (McCubbin, 2003).

Other researchers (Brown et al., 1999; Hamdi-Cherif, 2010; Imagined Futures: Capturing the Benefits of Genome Sequencing for Society, n.d.) point to more commercial uses in bioinformatics. These include, for example, biological modeling, gene sequence analysis, digital storage services for biological information, biological engineering, information selection and retrieval, participation in drug development, personalized medicine, and many other areas.

As for the legal regulation of the commercial use of the results of genomic research in the field of bioinformatics, it should be noted that there is currently no comprehensive regulation in this area. There is also no common approach, principles on the basis of which the consolidation, harmonization and development of legal regulation in this area would take place.

The lack of such a comprehensive legal regulation is quite understandable, since the results of bioinformatics research are manifested in various areas that were previously regulated. For example, legal status and protection of rights to computer programs and databases, copyrights, rights to inventions, industrial models, utility designs, protection of intellectual property. The same can be said about the regulation of relations in the field of information protection.

Nevertheless, the specifics of the field of genomic research leaves a serious imprint on the seemingly long-established relations and their legal regulation. That is why, in our opinion, it is necessary in this area to formulate general approaches and principles to legal regulation, based on which it would be possible to harmonize and consolidate legal regulation of the commercial use of the results of genomic research.

At the same time, in order to form effective legal regulation, in our opinion, it is necessary to smooth out the contradictions between the main points of collision of different interests in the field of genomic research, such as:

— correlation of the principle of freedom of scientific research with the need to ensure stability and security;

— correlation of various human rights among themselves;

— balance between the need to support development, progress and human rights;

— the relationship between the economic interests of large corporations and the rights of a particular person or groups of people (Astrelina, Kubyshkin and Kosilkin, 2019).

Also, as Sorokina (2020) justly notes, investment and commercialization of the genomic research industry is possible with a balance of human rights and non-discrimination, as well as in order to channel most of the profits into the further development of the scientific industry itself and scientific knowledge in the field of the human genome.

We also note that both legislative initiatives and judicial practice are just beginning to form balanced approaches to legal regulation and many questions and problems remain unresolved and are still subject to further development (D'yakov, 2020; Moskovkina, 2020; Ponomareva, 2020; Sorokina, 2020).

In this regard, attention is drawn to the proposal of the Committee on Ethics, Law and Society (CELS) of the Human Genome Organization (HUGO), within the framework of which a number of principles were formulated that, in the opinion of the representatives of the Committee, can form the basis of the regulatory model. The Committee formulated the following principles (Capps et al., 2019):

— social justice, within which the human genome is regarded as the common heritage of humanity, social justice in this case implies the right of every individual to share in the benefits of scientific progress and its technological applications;

— genomic solidarity. This principle implies that genomic research should be a reciprocal exchange between individuals and communities, with researchers, funders, and sponsors, so that all participants (human beings as originators of sequences) share in the benefits of the research through knowledge dissemination and progress, and not just as end-product users, for the reason that may create inequity because of commercial interests and differential access;

— work for the public good. Future regulatory models should be aimed at generating public social benefit and not merely private commercial gains.

These principles, in our opinion, are the most general principles of legal regulation and can be used as the basis for the regulatory model of commercial use of the results of genomic research; nevertheless, in our opinion, they need to be clarified and further developed in relation to specific areas of genomic research.

III. Biobanks Activities Issues

Examples of commercial use of the results of genomic research include the activities of biobanks and economic models of their functioning. Consideration of various approaches to economic models

of the functioning of biobanks will allow us to determine the approaches to the legal regulation of their activities, make assumptions about the legal nature of biobanks.

The variety of forms of activity of biobanks, the goals of their creation, the tasks that their founders set for the activities of biobanks, predetermines the variety of approaches to economic models of biobanks. Biobanking is a separate type of economic activity at the forefront of science, education and modern medical practice (Mokhov, 2018).

Often, a biobank is understood as a repository of various biological samples and materials (cells, tissues) (Mokhov, 2018). Meanwhile, it is important to change the approach — from a purely technical to a legal one, to endow biobanks with subjectivity, which implies licensing, control, and responsibility, to ensure the consistent implementation of the legal principles laid down in Russian legislation, which generally meet modern international standards, at all levels (Kosilkin, 2020).

A biobank is an object in the process of formation, the possible development paths of which can be a stake in numerous and diverse social conflicts unfolding around biobanks between social agents with their specific interests (scientists, doctors, states, investors, donors, groups of civil activists) (Varkhotov et al., 2016).

That is why the need to consider economic models for the functioning of biobanks seems to be the most urgent. In addition, when studying this issue, in our opinion, it is necessary to take into account modern civilizational tendencies affecting all spheres of social relations, including economics, law and others. As mentioned at the beginning of this article, this is a trend aimed at the formation of a post-industrial, information society, a post-industrial, information, digital economy.

When building an economic model of a biobank, it is necessary to take into account the following issues: understanding the market needs for the particular type of biobank under consideration, as well as understanding and efficiently managing the biobank "value chain", which includes the costs of sampling, tissue processing, storage, management, distribution of samples, infrastructure and administration (Vaught, Rogers, Carolin and Compton, 2011).

Depending on the goals and objectives, there are population biobanks and tissue biobanks, clinical and research biobanks (Hewitt and Watson, 2013; Loft and Poulsen, 1996).

Population biobanks include both epidemiological and clinical samples collected from volunteers without specific inclusion or exclusion criteria (Hubel, Spindler and Skubitz, 2014). Tissue biobanks are a source of data on the health status of the population (De Souza and Greenspan, 2013).

Depending on the owner of the property or depending on the founder, the biobank can be divided into state institutions, private organizations in any organizational and legal form, as well as mixed ones. It should be noted that, as a rule, this also determines the goals of the biobank as an independent structure. The activities of government agencies, as a rule, are not associated with the extraction of profit as the main goal. While the functioning of the biobank as a commercial structure, as a rule, is aimed primarily at making a profit. All this determines the economic models of the functioning of the corresponding structures. At the same time, we note that, for example, in relation to the Russian Federation, state institutions, as essentially non-profit organizations, have the right to carry out income-generating activities, provided that this serves to achieve the goals for which they were created, and if it corresponds to such goals.[5]

The economic models of the functioning of biobanks also differ accordingly. Thus, a biobank created by the state maintains its functioning mainly at the expense of state funds provided for one basis or another (subsidies, grants, donations, government contracts, budget investments, etc.).

A biobank, which functions as a private organization, mainly aims at making a profit, which predetermines the appropriate areas of activity and the need to build a marketing policy, communication with potential clients, minimize costs and expenses if it is necessary to increase margins, etc.

Meanwhile, the following should be noted. Biobank as an organization can pursue research goals, i.e. obtaining new scientific information as a result of analysis and processing of information contained in the biobank itself and attributable to the corresponding biological samples.

[5] p. 4, art. 50 of the Civil Code of the Russian Federation. Collection of Legislation of the Russian Federation, 1994, No 32, Art. 3301.

At the same time, maintaining the functioning of the biobank as an organization requires certain financial costs, which determines the commercial orientation of the biobank's activities.

Accordingly, in this situation, one can speak of a kind of biobank dualism, a special kind of dialectic that leads to the emergence of an internal contradiction in the activities of the biobank, which, nevertheless, can contribute to the development of this structure and the emergence of new qualities that can be used as competitive advantages in conditions of a market economy.

With regard to the post-industrial, information society, we can also talk about the information economy, in which the productivity and competitiveness of factors or agents (be it an individual, a firm, or a national economy) depends on the ability to generate, process and effectively use information based on knowledge (Tufetulov, 2017).

According to a number of scientists, a characteristic feature of the information economy is the formation of so-called network structures, network relations. The process of formation of the information economy changes the business environment and the dynamics of competition for all economic entities. Network structures and forms of management organize a space of close interaction between various spheres (technological, political, social, cultural) (Lazarev, Lazarev and Khizha, 2005).

One of the brightest technological manifestations of recent times is the blockchain information technology, the so-called distributed ledger technology.

Blockchain is a distributed database consisting of a "chain of blocks", block storage devices are not connected to a common server, the database allows controlling the reliability of transactions without supervision any financial regulators. Blockchain is a distributed and decentralized database formed by participants, in which it is impossible to falsify data due to the historical record and public confirmation of the transaction by all network participants (Fedotova, Yemel'yanov and Tipner, 2018).

Initially, this technology was used to form and circulate so-called cryptocurrencies. Nevertheless, this technology has a number of characteristics that make it possible to use it not only in the financial

sector, but also in other areas of society, for example, for notaries, cadastres, registers of property rights, taxes and benefits, violations and fines, user identification, registration of civil acts, civil status, public services, healthcare, education, art transfer, supplies, fair voting systems, loyalty programs, lotteries, etc. (Nagrodskaia, 2019).

The main characteristics of this technology that determine its attractiveness for use in various spheres of social relations are:

1) decentralization;

2) anonymity;

3) autonomy;

4) the use of cryptography;

5) adding special time stamps to each transaction (Nagrodskaia, 2019).

The idea of using blockchain technology in healthcare is not completely new. Currently, a number of projects based on the use of this technology are known, which have been successfully implemented and work in real life.

For example, Estonia became the first country to implement blockchain on a national scale. The eHealth Foundation of Estonia has been operating since 2005. In 2016, the eHealth Foundation teamed up with Guardtime, a data security company. Guardtime helped the foundation implement KSI (Keyless signature infrastructure), a blockchain technology that provides large-scale data authentication without relying on a centralized trusted authority. The project now contains over 1 million patient records and patient data. The KSI infrastructure ensures high security of medical data, their safety and integrity (Blockchain technologies application in health care, 2021).

The government of Mongolia, together with FarmaTrust Company, has launched a project to implement a drug tracking system based on blockchain technology, aimed at eliminating drug counterfeiting in the country (Mongolia to pilot blockchain drug traceability system, 2021).

The Novgorod Region became a pilot region in which, for the first time in Russia, Vnesheconombank (VEB) launched a program for monitoring drug circulation in a hospital using a blockchain system. This method of accounting will help fight counterfeiting and leakage of

expensive prescription drugs bought with budget money (Blockchain technologies to help control drugs trade in Nizhny Novgorod, 2021).

The use of blockchain technology is also possible in clinical trials in order to ensure the authenticity, reliability of results and to achieve other goals. Currently, the development of an information system for clinical trials based on blockchain technology is underway by a consortium, which includes the following organizations: National Medical Research Center of Oncology named after N.N. Petrov, National Medical Research Center of Oncology named after N.N. Blokhin, National Medical Research Center for Radiology, Ministry of Healthcare of the Russian Federation, First Saint Petersburg State Medical University named after academic I.P. Pavlov. The participants also include local ethics committees and patient organizations. The information system being created will improve the quality of clinical trials, ensure the availability and security of data, reduce the production time of modern anticancer drugs, and increase the level of technological equipment of the industry as a whole. The system will be validated according to international standards (Belyayev et al., 2018).

Foreign researchers also note the possible positive economic impact of the use of blockchain technology in medicine, healthcare, genomics, which is confirmed by a significant number of scientific studies devoted to this topic (Tandon, Dhir, Islam and Mäntymäki, 2020).

According to some authors, blockchain technology has become a suitable and modern solution for the secure storage and exchange of genomic data (Sami Ullah, Aslam and Arjomand, 2020). According to some studies, the market for the application of blockchain technology in the genomic market may grow at an average annual rate of 66.42 % for the period 2019–2029 (Research and Markets, 2019). Some authors suggest the possibility of using blockchain technology to create reliable systems for storing and processing genetic information (Ozercan, Ileri, Ayday and Alkan, 2018).

With regard to the functioning of biobanks, the use of blockchain technology will significantly improve business processes, increase the reliability of storage, processing and circulation of information, i.e. will make it possible to qualitatively change the means of production. Moreover, the use of blockchain technology will make it more convenient

for users and patients to work with the biobank, and will allow a more flexible use of the institution of informed consent.

Thus, when developing future economic models for the functioning of biobanks, it is advisable to take into account the possibility of using blockchain technology, which will significantly improve the organization of the biobank, rationalize the use of production means, and, consequently, obtain a significant economic effect from the introduction of appropriate technologies. Blockchain technology as applied to the economy of biobanks can be introduced both at the institutional and functional levels, and can be used in the formation of a special kind of regulatory environment for the activities of biobanks.

It is also necessary to note the possible positive effect of using blockchain technology for public administration in the field of biobanking and genomic research in general, in order to develop such a methodology for resolving ethical and other contradictions, which will allow making significant decisions in the field of genomic research in dynamics. In addition, in relation to the legal regulation of genomic research, the use of blockchain technology in the future may allow in real time to resolve controversial issues related to research in a pre-action manner.

An important aspect in the formation of an economic model for the functioning of biobanks is attracting investors to finance the activities of biobanks. In this area, a large number of behavior models are also possible, aimed at ensuring the rights of investors on the one hand, and at ensuring relative independence and a certain level of freedom in the activities of the biobank itself, on the other hand.

Within the framework of this paper, I would like to draw attention to new, only recently emerged, methods of financing activities, the development of which does not go unnoticed and increasingly affects the construction of certain economic models. This is, first, crowdfunding financing.

Crowdfunding is usually understood as such an activity when the relevant activities are financed not by the owner and not at the expense of the state, but at the expense of funds raised by persons in one way or another interested in a particular project.

Crowdfunding projects have been developing at a serious pace lately. According to the report of the research group Massolution, which collected data from 1,250 crowdfunding sites around the world, in 2015 its global volume was estimated at 34 billion US dollars, of which North America accounted for about half — 17.25 billion US dollars. Asia occupied the conditional second place with 10.54 billion US dollars; in Europe, they collected 6.48 billion US dollars (Motovilov, 2018).

For the first half of 2019, the volume of funding using the crowdfunding toolkit amounted to USD 6.923 billion. The Russian crowdfunding market over the past 5 years has grown more than 40 times in terms of funding. If in 2014 the total amount of financing for projects was only 0.3 billion rubles per year, then in 2018 the amount was about 14 billion rubles (according to the Bank of Russia estimates, from 13 to 15 billion rubles), and in 2019 it may reach 16 billion rubles. At the same time, the development of the market does not follow a linear trend, but exponentially. In the next 2 years, it is possible to expect more than a twofold increase in investments in the crowdfunding market, and in a 5-year perspective, according to the Bank of Russia forecast, the volume of crowdfunding financing will reach 1 trillion rubles in year (Neopulo, Popov and Kuksov, 2020).

Crowdfunding, as a way to attract funding, differs from both charity and classic investing. However, it is closely related to the specified methods of financing.

Initially, crowdfunding was formed as a non-investment, gratuitous model, when funds were transferred in the form of a donation (donation-based crowdfunding), as well as a model based on a kind of reward: non-financial or monetary (reward-based crowdfunding). Lending-based crowdfunding and equity crowdfunding have become more complex forms (Motovilov, 2018).

It is also very important to note the phenomenon of crowdfunding, in which fundraising in this way also has a fairly significant marketing effect, i.e. in this way, information about the relevant project is disseminated among a significant number of potential customers, which in the long term outlook can also have the necessary economic effect.

In addition, as a specific type of crowdfunding, one can consider such a method of financing, in which a client receives a service, for

example, information from a biobank, or analysis of certain information contained in a biobank in relation to a specific subject or object at a reduced price, but at the same time, the client provides biobank available and important for the biobank samples or data with certain conditions, allowing the biobank to use such samples or data on a fairly widespread basis.

In the Russian Federation, the Federal Law dated 02.08.2019 No 259-FZ "On attracting investments using investment platforms and on amending certain legislative acts of the Russian Federation"[6] is devoted to the legal regulation of certain types of crowdfunding. This law regulates only one type of crowdfunding, namely investment crowdfunding, or as it is also called, crowdinvesting. The law defines the basic concepts in this area, such as an investment platform, an operator of an investment platform, utilitarian digital rights and others, the law determines that the following digital rights (utilitarian digital rights) can be acquired, alienated and exercised in an investment platform: the right to demand transfer thing (things), the right to demand the transfer of exclusive rights to the results of intellectual activity and (or) the rights to use the results of intellectual activity, the right to demand the performance of work and (or) the provision of services. The law defines the requirements for an investment platform, an operator of an investment platform, an investor, a person attracting investments, an investment agreement, etc. The adoption of this law, despite some of its shortcomings, can be generally regarded as a positive fact that can contribute to the development of crowdfunding in the Russian Federation.

It can be assumed that crowdfunding as a way to finance the activities of biobanks is very promising and can receive serious development, given the great demand for the activities of biobanks. When constructing promising economic models for the functioning of biobanks, in our opinion, it is advisable to take into account the possibility of a similar method of financing. At the same time, it is likely that economic models using crowdfunding financing may also imply financing from investors, income from the activities of the biobank

[6] Collection of Legislation of the Russian Federation, 2019, No 31, Art. 4418.

itself and from other sources. Of course, this kind of financing will not be able to fully ensure reproduction in such a science-intensive and technological sphere of public life as biobanking, but it can be a significant help in financial support of the biobank's activities.

At the same time, when forming models of legal regulation of the activities of biobanks, it is necessary to take into account the approaches indicated above in this article to the formation of economic models of the activities of biobanks, including the possibility of using blockchain technologies and methods of crowdfunding financing. Taking into account the above tendencies will make it possible to form a model of legal regulation that best meets the modern realities of the information, post-industrial society, modern information, digital economy.

IV. Modern Challenges and Definition of Concepts in the Sphere of Legal Regulation of Genomic Research

In addition to the above factor associated with the formation of the information society, social relations in the field of genomic research are greatly influenced by the practical application of the results of scientific advances in medicine and biology.

The development of modern technologies and modern challenges, such as the possibility of genome editing using CRISPR-Cas9 technology, the possibility of implementing mitochondrial replacement therapy methods and using these methods in practice, the possibility of the so-called intracytoplasmic injection of male germ cells, the ability to examine embryos for the presence of genetic diseases, the relative prevalence of donation of male germ cells, eggs, embryos and the use of the corresponding cells in assisted reproductive technologies have largely affected the spheres of social relations associated with donation and parenthood, which often leads to ambiguous legal situations.

So, in 2019, the following situation was considered in the courts of England: a man (ex-woman), known only as TT, was fertilized with donor sperm in order to conceive a child, named only as YY in court documents. He wants to be called "father" or "parent" of YY on his birth certificate, but because he suffered a pregnancy, he is designated as a mother under the Human Fertilization and Embryology Act 1990

(Human Fertilisation and Embryology Act 1990, 2021). The fact is that TT is transgender and received documents on gender reassignment before treatment, therefore, legally he is a man (Judge calls for law review after trans man gives birth — BioNews, 2021).

Therefore, within the framework of this article, we will focus on the definition of approaches to the formulation of such basic concepts in the field of human reproduction as donation and parenthood.

Approaches to legal regulation in the field of genetic research of human reproduction should ensure a balance of public and private interests, the interests of various actors involved in relevant social relations, a balance between personal and public interests.

To form a full-fledged legal regulation in any area, it is initially necessary to clearly define the concepts that will appear in the normative legal acts devoted to the regulation of the relevant social relations, as well as used in the doctrine.

The formation of the conceptual apparatus is necessary to ensure certainty, accuracy, unambiguity of the legal regulation of the relevant social relations. Scientifically grounded and clearly formulated concepts set the direction of regulation both in positive law and in doctrine, and define the boundaries of such regulation.

The legislation of the Russian Federation contains a definition of a donor of biological material. However, this definition applies only to the field of biomedical cell products, regulated by the relevant law, which does not apply to relations arising from the use of human germ cells for using assisted reproductive technologies, as well as to relations arising from the circulation of cells and human tissues for scientific and educational purposes.[7] With regard to the field of human reproduction, the concept of a donor should be clarified, since the legal status of a donor in the field of human reproduction differs significantly from the status of a donor of other biological materials.

In foreign legal acts (Health & Consumer Protection Directorate-General of the European Commission, 2006; Sabatello, 2015) the concept of a donor is widespread as a person who has provided his

[7] Federal Law No 180-FZ dated 23.06.2016 (as amended on 03.08.2018) "On Biomedical Cell Products", Art. 1. Collection of Legislation of the Russian Federation, 2016, N 26 (Part I), Art. 3849.

reproductive cells for medical purposes. In each case there are different options for definitions, which emphasize different aspects.

For example, in the UK, the Donor Disclosure Regulation 2004 No 1511, adopted on June 14, 2004[8] a donor is defined as a person who has provided the sperm, eggs or embryos that have been used for treatment services in consequence of which the applicant was, or may have been, born. At the same time, in the UK Human Fertilization and Embryology Act 1990 (Human Fertilisation and Embryology Act 1990, 2021) there is particular emphasis on the fact that the donor's consent must be obtained for the use of the appropriate cells: A person's gametes should not be used for treatment or non-medical fertility treatment services unless that person has valid consent to their use and they are used in accordance with terms of consent. A person's gametes should not be accepted for use for these purposes, unless that person has actual consent to use them.

A more comprehensive definition of a donor in human reproduction is found in the Children and Family Relationships Act 2015, Section 4 of Part 2:[9]

"donor"—

(a) in relation to a gamete, means-

(i) a person who has consented, under section 6 or in the manner referred to in section 26 (1)(b)(ii), to the use in a DAHR procedure of a gamete provided by him or her, or

(ii) the donor of a gamete to which section 26 (6) applies,

and includes a donor of a gamete that is used in the formation of an embryo that is used in a further DAHR procedure, and

(b) in relation to an embryo, means-

(i) a person who has consented under section 14 or 16 or in the manner referred to in section 26 (2)(b)(ii), to the use of the embryo in a DAHR procedure or a further DAHR procedure, or

[8] 2004 No 1511 The Human Fertilisation and Embryology Authority (Disclosure of Donor Information) Regulations 2004. Available at: http://www.legislation.gov.uk/uksi/2004/1511/pdfs/uksi_20041511_en.pdf [Accessed 22.03.2021].

[9] Children and Family Relationships Act 2015. Available at: http://revisedacts.lawreform.ie/eli/2015/act/9/revised/en/html#SEC26, http://www.irishstatutebook.ie/eli/2015/act/9/enacted/en/html.

(ii) the donor of an embryo to which section 26 (6) applies.

As you can see, in this definition, the main emphasis is on obtaining the consent of the donor for the provision of the corresponding cells, and the said Law also states that the donor must provide certain information without fail: his or her name; his or her date and place of birth; his or her citizenship; the date and place at which he or she provided the gamete; his or her contact details (clause 24 (3) part 3).

An analysis of the regulation of donation of reproductive cells in different countries suggests that the donor definition should necessarily reflect the subject of donation, i.e. what specific cells and/or materials are provided (female germ cells, male germ cells, embryos), for what purposes (for example, in vitro fertilization, other assisted reproductive technologies, etc.), subject to the availability of appropriate consent to these procedures, and also subject to the provision of the necessary information. Other required parameters may be reflected in the definition.

Among the rights of the donor, the question of whether the donor has (or can have) any parental rights in relation to children born as a result of his donation is quite controversial.

As a general rule, a donor should not have such rights in relation to children born as a result of his donation. However, under certain conditions, such rights may arise from the donor. Thus, we come to the definition of parenthood. The concept of parenthood, legal ties between parents and children are of great importance not only in terms of ensuring children's rights, but also in terms of property issues, inheritance issues, etc.

In the Russian Federation, for example, Art. 48, 51 of the Family Code of the Russian Federation[10] and Chapter II of the Federal Law dated 15.11.1997 No 143-FZ "On acts of civil status"[11] are devoted to these matters. For example, in accordance with Art. 51 of the Family Code of the Russian Federation, persons who are married and who have given their written consent to the use of the method of artificial insemination or to the implantation of an embryo, in the event that they have a child

[10] Collection of Legislation of the Russian Federation, 1996, No 1, Art. 16,

[11] Collection of Legislation of the Russian Federation, 1997, No 47, Art. 5340.

as a result of the use of these methods, are recorded by their parents in the birth register. Persons who are married to each other and have given their written consent to implantation of an embryo to another woman for carrying it, can be registered as the child's parents only with the consent of the woman who gave birth to the child (surrogate mother). As we can see, these definitions are rather limited in nature, they only regulate situations that arise in persons who are in a registered marriage, and do not regulate various other situations.

The issues of determining parenthood have been studied in sufficient detail within the framework of the Hague Conference on Private International Law since 2011 (HCCH. The Parentage/Surrogacy Project, 2021). As part of this work, in 2014 the document "Desirability and Feasibility of Further Work on the Parentage/Surrogacy Project" (2021)[12] was approved, which summarizes the work on the project over the past period and formulates proposals for the following periods. The concept of parenthood within the framework of this project is considered in relation to ensuring children's rights in the light of human rights in general, private legal aspects of relationships complicated by a foreign element are considered. Within the framework of the project, definitions of legal parenthood or legal parents are formulated, which are understood as a person (persons) who have acquired the legal status of the child's "parents" in accordance with the relevant law, and who will receive all the rights and obligations arising from this status in accordance with this law. The concept of genetic parenthood or genetic parents is also formulated: a person (persons) who provided their genetic material for conceiving a child. In some languages this is called "biological origin." Within the framework of the project, annual conferences are held, according to the results of which the corresponding reports are adopted.

In parenthood, three main aspects can be distinguished, two of which apply to both men and women, namely: the genetic aspect and the intentional aspect (intentions), and one only to women is the gestational aspect.

Some of the researchers believe that parenthood intent is, in fact, an aspect of parenthood that supports full recognition of parenthood

[12] Available at: https://assets.hcch.net/docs/6403eddb-3b47-4680-ba4a-3fe3e11c0557.pdf [Accessed 22.03.2021].

with the exception of genetic or gestational input or marital assumptions (Storrow, 2002). Nevertheless, in our opinion, it is necessary to take into account various factors and use an integrated approach to the definition of parenthood in the field of reproductive technologies, while, of course, intention is of great importance in this matter.

V. Ensuring a Balance of Interests as the Basis for Legal Regulation of Social Relations in the field of Genomic Research

It seems important from the point of view of the formation of legal regulation in the field of genomic research, to dwell a little on such an issue as ensuring a balance of interests as the basis of legal regulation in this area.

Recently, it is often possible to meet the opposition of human life and health on the one hand and the interests of science and society on the other. Meanwhile, in our opinion, such opposition leads to a negative effect in any case, no matter which of the interests is put at the forefront. It seems that ensuring a balance of interests, both legal and organizational, can be considered as the basis of legal regulation in this area, so I would like to dwell a little on this issue.

Interest is characterized as something objectively significant, necessary for an individual, collective, society, etc. (Philosophical Dictionary, 1980, p. 131). At the same time, interest in law serves as its most important law-forming and law-implementing factor (Kosarenko, 2007).

With regard to the area under consideration, three levels of interests can be distinguished according to the degree of their commonality — these are private interests, group interests and general or, in other words, public interests.

Among the private interests, first, it is necessary to note the interests of specific people, individuals who, within the framework of the considered social relations, can act in various qualities — a patient, a participant in scientific research, etc. It seems that the main, legally significant direction, vector of private interests is the provision of individual rights and freedoms of individuals.

With regard to group interests, the interests of various social groups or group social players can be named as subjects. In the area under consideration, these include, for example, the interests of business, entrepreneurs, incl. large medical and/or pharmaceutical corporations, which are characterized by an independent focus, first, on maximizing profit and often come into conflict with the interests of individuals and even with public interests.

Public interests can be attributed to the state, the purpose of which should be, first, to ensure the stability and security of the development of society, to maintain public consensus and balance, which determines the direction, vector of interest in this case.

Thus, it is obvious that there are at least three levels of interests, which often come into conflict with each other and need to find a balance.

It seems that when determining approaches to determining the balance of interests in this case, the following factors should be taken into account.

1. The dynamic development of the regulated sphere of social relations, due to the explosive development of technologies in the field of genomic research in recent years.

2. Extreme sensitivity of the relevant sphere of social relations, including in relation to a specific person, especially when it comes to genomic research in the field of human reproduction.

3. A significant number of relations between subjects of different states in the considered sphere of social relations.

4. Close connection of the considered sphere of social relations with human rights law as an independent branch of international law.

5. Significant influence of ethics and morality on social relations in this area.

Taking into account these factors, it can be assumed that in order to ensure a balance of private, group and general interests, it is necessary to establish sufficiently clear and developed norms in positive law, including at the level of international law and the law of interstate integration formations, it is necessary to use a symbiotic regulator, including both legal norms and norms of a different social nature. In addition, there is a need for a credible and reliable mechanism that would make it possible to promptly resolve emerging issues and contradictions of both ethical and legal nature.

VI. Conclusion

Based on the results of considering the issues indicated in this article, the following conclusions can be drawn.

The development of an informational, post-industrial society, informational, digital economy is an important factor that has determined the emergence of new areas of knowledge, scientific disciplines, new challenges, including in the field of genomic research. In particular, such a scientific discipline as bioinformatics has appeared and is rapidly developing. Legal regulation of social relations in the field of bioinformatics should take into account the substantial dualism of information and, in this regard, may be a combination of international legal regulation and (or regulation at the level of regional integration formations) and harmonization of legislation and legal regulation of various states.

Biobanks are the most pronounced industry in the field of the implementation of the results of genomic research, which has been rapidly developing lately, which requires the formation of a scientifically based model of legal regulation of the activities of biobanks taking into account the current state of economic relations.

At the same time, it is advisable to take into account the possibility of using blockchain technology, which can significantly improve the organization of the biobank, rationalize the use of means of production, and, therefore, obtain a significant economic effect from the introduction of appropriate technologies. Blockchain technology as applied to the economy of biobanks can be introduced both at the institutional and functional levels, and can be used in the formation of a special kind of regulatory environment for the activities of biobanks.

It is also necessary to note the possible positive effect of using blockchain technology for public administration in the field of biobanking and genomic research in general, in order to develop such a methodology for resolving ethical and other contradictions, which will allow making significant decisions in the field of genomic research in dynamics. In addition, in relation to the legal regulation of genomic research, the use of blockchain technology in the future may allow in real time to resolve controversial issues related to research in a pre-trial manner.

Crowdfunding, as a way to finance the activities of biobanks, is very promising and can get serious development, given the great demand for the activities of biobanks. When constructing promising economic models for the functioning of biobanks, in our opinion, it is advisable to take into account the possibility of a similar method of financing. At the same time, it is likely that economic models using crowdfunding financing may also imply financing from investors, income from the activities of the biobank itself and from other sources. Of course, this kind of financing will not be able to fully ensure reproduction in such a science-intensive and technological sphere of public life as biobanking, but it can be a significant help in financial support of the biobank's activities.

Social relations in the field of genomic research are greatly influenced by the practical application of the results of scientific advances in medicine and biology. The development of modern technologies and modern challenges, such as the possibility of genome editing using CRISPR-Cas9 technology, the possibility of implementing mitochondrial replacement therapy methods and using these methods in practice, the possibility of the so-called intracytoplasmic injection of male germ cells, the ability to examine embryos for the presence of genetic diseases, the relative prevalence of donation of male germ cells, eggs, embryos and the use of corresponding cells in assisted reproductive technologies, largely affected the spheres of social relations associated with donation and parenthood, which makes it necessary to propose approaches to the formulation of relevant concepts as a basis for legal regulation in the specified area.

To ensure a balance of private, group and general interests, it is necessary to establish sufficiently clear and developed norms in positive law, including at the level of international law and the law of interstate integration formations, it is necessary to use a symbiotic regulator, including both legal norms and norms of a different social nature. In addition, there is a need for a credible and reliable mechanism that would make it possible to promptly resolve emerging issues and contradictions of both ethical and legal nature.

Legal regulation of genomic research presupposes a comprehensive regulation of relevant social relations, within which it is necessary to

take into account modern challenges, achievements of other sciences and disciplines in order to propose models of legal regulation that most closely meet the needs of modern society.

References

1. Astrelina, T., Kubyshkin, A. and Kosilkin, S., (2019). International legal regulation of genetic research, biobanking, bioinformatics and human reproduction: Analysis of the main international legal acts. *International Legal Courier, International Law and Human Genome Research*, 2–3(31–32), pp. 29–34. (In Russ.).

2. Bell, D., (1999). *The Coming Post-Industrial Society: The Experience of Social Forecasting*. Moscow: Academia. (In Russ.).

3. Belyayev, A., Stilidi, I., Kaprin, A., Lichinitser, M., Mescheryakov, A., Semiglazov, V., Imyanitov, E., Semiglazova, T., Poltoratsky, A., Konstantinov, L., Petrusenko, I., Nikitin, O., Zakharov, K., Trifonov, M. and Plakhov, D., (2018). Blockchain in healthcare: opportunities for use in clinical trials. *Lechbnoe delo*, 2. (In Russ.).

4. Bionews.org.uk. (2021). *Judge calls for law review after trans man gives birth — BioNews*. [online] Available at: https://www.bionews.org.uk/page_141465 [Accessed 22.03.2021].

5. Brown, N., Nelis, A., Rappert, B., Webster, A. and Ommen van, G., (1999). *Bioinformatics: A technology assessment of recent developments in bioinformatics and related areas of research and development including high throughput screening and combinatorial chemistry*. [online] Final Report for the Science and Technological Options Assessment (STOA) Unit, European Parliament. Available at: https://www.europarl.europa.eu/RegData/etudes/etudes/join/1999/167885/DG-4-JOIN_ET(1999)167885_EN.pdf [Accessed 15.11.2020].

6. Capps, B., Chadwick, R., Joly, Y., Lysaght, T., Mills, C., Mulvihill, J. and Zwart, H., (2019). Statement on bioinformatics and capturing the benefits of genome sequencing for society. *Human Genomics*, 13(1).

7. Capps, B., Chadwick, R., Joly, Y., Lysaght, T., Mills, C., Mulvihill, J. and Zwart, H., (2019). Statement on bioinformatics and capturing the benefits of genome sequencing for society. *Human Genomics*, 13(1).

8. De Souza, Y. and Greenspan, J., (2013). Biobanking past, present and future. *AIDS*, 27(3), pp. 303–312.

9. Digiforest.io. (2021). *Blockchain technologies application in health care*. [online] Available at: https://digiforest.io/blog/blockchain-examples-in-healthcare [Accessed 8.012021].

10. D'yakov, V., (2020). Unauthorized use of genomic information as a 21st century crime. In: *21st International Scientific Conference "The Civilizational Role of Law in Modern Integration Processes"*. Moscow: World of Science. (In Russ.).

11. Ermishina, E., (1988). *International exchange of information: Legal aspects*. Moscow: Mezhdunar. otnosheniia, p. 13. (In Russ.).

12. Fedotova, V., Yemel'yanov, B. and Tipner, L., (2018). The concept of blockchain and the possibilities of its use. *European Science*, 1(33). (In Russ.).

13. Hamdi-Cherif, A., (2010). Intelligent Control and Biological Regulation for Bioinformatics. *International Journal of Mathematical Models and Methods in Applied Sciences*, 2(4), pp. 93–104.

14. Hcch.net. (2021). HCCH. The Parentage/Surrogacy Project. [online] Available at: https://www.hcch.net/en/projects/legislative-projects/parentage-surrogacy [Accessed 22.03.2021].

15. Health & Consumer Protection Directorate-General of the European Commission, (2006). *Report on the Regulation of Reproductive Cell Donation in the European Union*. [online] European Commission. Available at: https://ec.europa.eu/health/archive/ph_threats/human_substance/documents/tissues_frep_en.pdf [Accessed 10.01.2021].

16. Hewitt, R. and Watson, P., (2013). Defining Biobank. *Biopreservation and Biobanking*, 11(5), pp. 309–315.

17. Hubel, A., Spindler, R. and Skubitz, A., (2014). Storage of Human Biospecimens: Selection of the Optimal Storage Temperature. *Biopreservation and Biobanking*, 12(3), pp. 165–175.

18. *Imagined Futures: Capturing the Benefits of Genome Sequencing for Society*. [ebook]. (n.d.). Available at: http://www.hugo-international.org/Resources/Documents/CELS_Article-ImaginedFutures_2014.pdf [Accessed 21.03.2021].

19. Kosarenko, N., (2007). Category "interest" in the system of public and private law. *Knowledge. Understanding. Skill*, 3, p. 157. (In Russ.).

20. Kosilkin, S., (2020). Experience of legal regulation of biobank activities in foreign practice and the development of Russian legislation. *Courier of Kutafin Moscow State Law University (MSAL)*, 4, pp. 79–87. (In Russ.).

21. Lazarev, I., Lazarev, K. and Khizha, G., (2005). New information economy and network mechanisms of its development. *Economic strategies*, 8. (In Russ.).

22. Legislation.gov.uk. (2021). Human Fertilisation and Embryology Act 1990. [online] Available at: https://www.legislation.gov.uk/ukpga/1990/37/contents [Accessed 22.03.2021].

23. Loft, S. and Poulsen, H., (1996). Cancer risk and oxidative DNA damage in man. *Journal of Molecular Medicine*, 74(6), pp. 297–312.

24. Lopatin, V., (2000). *Information Security in Russia: Man. Society. State*. Sankt-Peterburg: Universitet, p. 27. (In Russ.).

25. McCubbin, C., (2003). Legal issues in bioinformatics. *Journal of Commercial Biotechnology*, 9(3), pp. 249–265.

26. *Modern dictionary of foreign words*, (1993). Moscow, p. 254. (In Russ.).

27. Mokhov, A., (2018). Biobanking — A new direction of economic activity. *Courier of the Kutafin Moscow State Law University (MSAL)*, 3. (In Russ.).

28. Moskovkina, E., (2020). Protection of the right to inviolability of private life in the context of the development of genetic technologies. In: *Civilization of knowledge: Russian realities. 21st International Scientific Conference*. Moscow: World of Science. (In Russ.).

29. Motovilov, O., (2018). Crowdfunding phenomenon: investigation of features. *St Petersburg University Journal of Economic Studies*, 34(2). (In Russ.).

30. Nagrodskaia, V., (2019). *New technologies (blockchain/artificial intelligence) in the service of law: scientific and methodological manual*. Moscow: Prospekt. (In Russ.).

31. Neopulo, K., Popov, I. and Kuksov, A., (2020). Trends and prospects for the implementation of crowdfunding as a way of financing investment projects in Russia. *Vestnik Universiteta*, 1, pp. 129–136. (In Russ.).

32. Ozercan, H., Ileri, A., Ayday, E. and Alkan, C., (2018). Realizing the potential of blockchain technologies in genomics. *Genome Research*, 28(9), pp. 1255–1263.

33. Ozhegov, S., (1990). *Dictionary of the Russian language*. 22nd ed. Moscow, p. 253. (In Russ.).

34. *Philosophical Dictionary*, (1980). Moscow, p. 131. (In Russ.).

35. Plakhotnoy, D. ed., (1992). *Socio-economic nature of the information product and information resource*. Moscow: Publishing house of Moscow State University, p. 16. (In Russ.).

36. Ponomareva, D., (2020). Discrimination based on genetic status and the practice of the USA and Canada. In: *Civilizational role of law in modern integration processes. 21st International Scientific Conference*. Moscow: World of Science. (In Russ.).

37. Rayzberg, B., Lozovskiy, L. and Starodubtseva, E., (2011). *Modern Economic Dictionary*. 6th ed. Moscow: Infra-M. (In Russ.).

38. Research and Markets, (2019). *Blockchain in Genomics. Global Market Analysis Through 2019–2029, Projecting a CAGR of 66.42 %*. [online] GlobeNewswire News Room: Research and Markets. Available at: http://www.globenewswire.com/news-release/2019/10/22/1933431/0/en/Blockchain-in-GenomicsGlobal-Market-Analysis-Through-2019-2029-Projecting-a-CAGR-of-66-42.html [Accessed 10.01.2021].

39. Sabatello, M., (2015). Regulating Gamete Donation in the U.S.: Ethical, Legal and Social Implications. *Laws*, 4(3), pp. 352–376.

40. Sami Ullah, H., Aslam, S. and Arjomand, N., (2020). Blockchain in Healthcare and Medicine: A Contemporary Research of Applications, Challenges, and Future Perspectives. [online] Available at: https://arxiv.org/abs/2004.06795 [Accessed 20.03.2021].

41. Securingindustry.com. (2021). *Mongolia to pilot blockchain drug traceability system*. [online] Available at: https://www.securingindustry.com/pharmaceuticals/mongolia-to-pilot-national-blockchain-drug-traceability-system/s40/a8869/#.X1aR33kzZPZ [Accessed 08.012021].

42. Sorokina, E., (2020). Investment activity in the field of the human genome: achieving a high effect and possible risks on the example of judicial practice. In: *Civilization of knowledge: Russian realities*.

21st International Scientific conference. Moscow: World of Science. (In Russ.).

43. *Soviet encyclopedic dictionary*, (1989). 4th ed. Moscow, p. 504. (In Russ.).

44. Storrow, R., (2002). Parenthood by Pure Intention: Assisted Reproduction and the Functional Approach to Parentage. *Hastings Law Journal*, [online] 53, p. 597. Available at: https://repository.uchastings.edu/hastings_law_journal/vol53/iss3/2 [Accessed 08.012021]. (In Russ.).

45. Tandon, A., Dhir, A., Islam, A. and Mäntymäki, M., (2020). Blockchain in healthcare: A systematic literature review, synthesizing framework and future research agenda. *Computers in Industry*, 122, p. 103–290.

46. TASS. (2021). *Blockchain technologies to help control drugs trade in Nizhny Novgorod*. [online] Available at: https://tass.ru/ekonomika/5123036 [Accessed 21.03.2021].

47. Tufetulov, A., (2017). Information economy and information society. *Actual Problems of Economics and Law*, 3(3), pp. 39–46. (In Russ.).

48. Varkhotov, T., Gavrilenko, S., Stambolskii, D., Ogorodova, L., Bryzgalina, E. and Alasaniia, K., (2016). The tasks of social and humanitarian support for the creation of a national depository bank for biomaterials in Russia. *Problems of Philosophy*, 3. (In Russ.).

49. Vaught, J., Rogers, J., Carolin, T. and Compton, C., (2011). Biobankonomics: Developing a Sustainable Business Model Approach for the Formation of a Human Tissue Biobank. *JNCI Monographs*, 42, pp. 24–31.

50. Wiener, N., (1958). *Cybernetics and society*. Moscow, p. 31. (In Russ.).

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ARTICLES

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Bioethics and Biolaw as Bioeconomy Regulators

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Abstract: The paper deals with the ethical and legal principles (foundations) of economy that have been important and required to a various extent at different stages in history. Advances in science and technology, emergence of modern biotechnologies, including the genetic ones, as well as shifts to new technological paradigms, on the one hand, make the emerging economy drift towards bioeconomy, and, on the other hand, increase the need for legal and ethical regulators. In view of the above, bioethics and biolaw begin to play an increasingly active role at the new stage of human civilization development. In Russia, the phenomena of *bioethics* and *bio-law* are at the initial stage of their institutionalization, they become more and more appealing due to the intensification of public debates, as well as due to an increase in the number of conflicts caused by the attempts to implement and broadly apply the achievements of biology, medicine and other sciences about life in daily practice.

Keywords: economy, bioeconomy, ethics, bioethics, law, biolaw, technologies, conflicts, the concept of four "BIOs", regulation, biopolitics

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Contents

I. Introduction

Throughout almost the entire history of human civilization development — at least since the emergence of states — economy, to various extents, has been exposed to some influence, attempts to regulate the social relations most significant for the political and (or) economic elites. Imposition of taxes, fees, and other charges, as well as the economic relations between the state and the church, or the state and the neighboring countries, have been inevitably fixed in certain rules, laws and other regulations. At the same time, most of the routine economic issues have been left to the discretion of such regulators as morality, religion, and ethics due to their significant role in traditional societies. Economy has been "included" in daily life (Ivashkovsky, 2011), rather than opposed to it.

The relative gap between society, the institutions thereof, and economy began to emerge in the Middle Ages and reached its climax by the 20th century. Private interest became the key driver, and economic resources (land, labor, capital) became the limiter. To a certain extent, the state could act as a regulator, catering to the most significant public interests, and limiting certain types of economic activity (with evidently negative social consequences). However, overall, the achievement of the nearest economic goal was generally no longer associated with an ethical choice. This issue was left to the discretion of the authorities, the legislators.

However, the processes and the events negative for human civilization (the struggle of workers for their social rights, revolutions,

world wars, economic downturns, and sometimes even economic depressions, etc.) forced scientists to once again pay attention to the ethical and legal aspects of supporting economic activity, as well as to the need for a balanced policy in the state (not only in terms of economy, but also in terms of other aspects such as demography, family, migration, etc.).

An individual is not only a subject of certain economic relations (labor, management, or property ones), but also an active participant in non-economic relations. By mid-20th century, technologies had already provided the opportunity to significantly reduce the working day duration, and to form the sphere of consumption and leisure. Various service markets have begun to grow fast, and employment has been rapidly changing. An individual has been increasingly pushed out of the economic turnover, becoming an active consumer of services, rather than a producer of goods.

In the second half of the 20th century, bioethics and medical law began to stand apart as responses to biotechnological challenges, as well as due to the evident need for social control over medical professionals, and (later) biologists. Unless decisive measures are taken, the primacy of economic interests over any others (social, environmental, etc.) can lead to irreversible consequences for certain states, regions, and even humanity as a whole, within the next few years.

II. Bioeconomy as a Phenomenon

Much has been written about bioeconomy and its "sprouts". Currently, there are different approaches to understanding bioeconomy.

Bioeconomy is the sustainable controlled conversion of biomass into a range of food, health, and industrial products, as well as energy (BECOTEPS. The European Bioeconomy in 2030 — Delivering Sustainable Growth by addressing the Grand Societal Challenges, n.d.).

Bioeconomy is a biobased, renewables-based, sustainable economy (Brunori, 2013).

Bioeconomy is a branch of social science that integrates the disciplines (and knowledge) of economics and biology in order to solve its own problems and to create a coherent theory explaining the events

and processes occurring in connection with the development of new biotechnologies (Mateescu et al., 2011).

Despite some differences in approaches to understanding bioeconomy, it is based on an emerging biotechnological platform which is unique for the current time in history and allows, along with other modern (digital, management, etc.) technologies, both creating absolutely new products (goods, works, services), and significantly influencing the existing ones. Biotechnologies stimulate development of new segments and/or sectors of economy, have a significant impact on the processes and the speed of modernization of the existing ones (especially in high-tech sectors/segments) (Schwab, 2016), and are capable of boosting business activity in the traditional industries and sectors of economy, i.e., have serious innovative, multiplier and other effects.

Biomedicine and biopharmaceutics, agriculture, food industry, as well as bioenergy sector have the highest potential for development. A good potential for development exists in the IT sector facilitating the exchange of bio-data, and genetic or other information about humans, plants, animals. There are also some prospects for the introduction of certain biotechnologies in the environmental sector.

The main driver of the emerging bioeconomy as a whole, as well as its individual industries and sectors, are biotechnologies and other technologies (medical, digital, etc.) generating a synergistic effect when used together. The already existing, as well as the potential capabilities thereof evidence the emergence of not only breakthrough, but also disruptive innovations, that allow not only significantly improving the products circulating in the market, but also changing the production, technological and even some social processes.

Bioeconomy is a slowly emerging economy of a new type, characterized not only by active exploitation of biotechnologies and bioresources (which is typical for any economy), but also by the use of such technologies and resources following scientifically sound principles which ensure the rational use thereof, the "closed-loop" lifecycles of biotechnologies and other technologies, therefore allowing minimization of the negative impact of various factors on the environment, the biosphere.

So far, it looks like an experimental economy with unclear actual long-term prospects, and sometimes even like science fiction (in terms of closed-loop cycles, full reproduction, effective management of environmental and other risks). However, the objective laws of nature will sooner or later force the human civilization to follow the path of practical implementation of the concept of three (biotechnology — biosafety — bioeconomy) or even four (biotechnology — biosafety — bioeconomy — biopolitics) "BIOs" (Mokhov, 2020), and bioethics and bio-law, most likely, will soon become the regulatory basis therefor and remain so for decades. In this instance, it is important not to waste time in order to prevent serious mistakes that can discredit the really useful technologies, by timely drawing a line of demarcation between the useful technologies and the harmful or "questionable" ones (including the products obtained through the use thereof).

Some countries (UK, USA, etc.) (BBSRC, Biotech Britain, 2015) expect a rapid growth of bioeconomy over the next decade, along with weakening of the role and importance of the traditional industries and sectors both in economy and in politics.

Due to the novelty of the phenomenon under consideration, the word "bioeconomy" is not often mentioned in laws, regulations and other national documents. Resolution of the Government of the Russian Federation No 316 of 15 April 2014 entitled *Approval of the "Economic Development and Innovative Economy" State Program of the Russian Federation* pointed out the need for a transition from individual measures in support of the sphere to formation of an integral system for the development of bioeconomy in Russia. The term "bioeconomy" was also mentioned in other documents that are no longer valid.[1]

While some time ago the economic policy was determined by landowners, then by industrialists, and now — almost everywhere — by bankers, they may soon start to be squeezed out by the proteges of biotech

[1] Rasporyazheniye Pravitel'stva RF ot 27.12.2012 № 2539-r "O gosudarstvennoy programme RF 'Razvitiye promyshlennosti i povysheniye yeye konkurentosposobnosti'" [Order of the Government of the Russian Federation No 2539-r dated 27 December 2012 *On "Industry Development and Competitiveness Increase" State Program of the Russian Federation*]. Collection of Legislation of the Russian Federation, 2012, No 53 (Part II), Art. 8043.

companies. On the one hand, this is a natural process for innovative technologies development (intellectual work and innovation are being actively supported at the official level in many countries, while "money bags" — under various pretexts, although not always successfully — are being pushed away from making key political decisions due to the obvious contradictions between the capital and the labor), however, on the other hand, a rapid expansion of new entities into the economic and (or) political elites may lead to imposition of wrong priorities on the society through laws and administrative procedures, which will manifest itself in a biased, unbalanced biopolitics, and cause a serious social conflict.

It is not a mere coincidence that — despite the innovative, experimental nature of certain technologies and solutions — scientists, experts, and policymakers are already raising and discussing the issues of ensuring biological and other kinds of safety/security. Decoding of the human genome, as well as the genomes of many animals and plants, digitalization of considerable amounts of genetic information, the possibilities opened up by the actively developing synthetic biology and other directions of science and technology advancement allow extensive intervention into the human and/or animal genome, creation of chimeras, biological objects with predetermined programmable properties, as well as a "synthetic genome" or fragments thereof which can be introduced into a biological object and make possible its subsequent reprogramming, or transformation. Such technologies open up vast prospects for agriculture, industry, medicine (including veterinary), and pharmaceutics. However, haphazard, not properly thought through, decisions, the "race for the genome", for scientific (research) and other kinds of success at any cost may entail serious problems of a biological, social and economic nature. Besides, we must not forget about the existence of formal and non-formal groups trying to achieve their political, military and other goals using technological advances and advantages.

Knowing the ethnic and other collective characteristics of [geographically] concentrated communities, one can try creating a "selective" weapon. Such attempts are being made in the USA, China, Japan, and some other countries. The corresponding research and

development may be financed by both NGOs and individuals. The research is taking place in the following areas: modifications of highly dangerous infectants; production of latent viruses, genetic elements (introduced on viruses); production of new toxins (with higher resistance and virulence); synthesis of new biological compounds (bio-poisons).

The control over military biorobots, as well as artificial intelligence systems aimed at causing harm to human health or life, and the environment, are becoming a separate problem.

In view of the above, the countries all over the world are facing the need to promptly resolve the issues of ensuring biosafety, creating biological risk management systems, performing comprehensive assessment of biotechnologies, monitoring new technologies and biological objects.

The principle of precaution known in international, medical, and environmental law acquires a new perspective, requiring development of a set of measures in order to ensure its implementation and application in practice.

A number of fundamental challenges also exist in the development of bioeconomy as a whole (from modernization or disruption of the prevailing global and national economic models, to the shift of the macroeconomic and social processes management paradigm). The existing challenges and threats to civilization are becoming so obvious that they must not be ignored, although the current daily problems facing the policymakers and governments focused on solving short-term national issues make them actively resort to the "avoidance" technique. This results in decades of unproductive work of experts consisting in development of recommendations, "roadmaps", and similar documents, which, as a rule, are neither universally binding, nor supported by the necessary enforcement or other efficient mechanisms. Consequently, governmental and nongovernmental entities and institutions fail to respond even to insignificant new or unconventional challenges and threats.

Along with the old (and still outstanding) problems related to the functioning of economic entities, businesses, and their harmful activities (at least from the standpoint of ecology, environmental pollution), new ones are coming up. The power resource of science and technology is

steadily increasing; the opportunities for managing the conception of life (birth), as well as the lifecycle of living systems (including dying and death) are emerging. Importantly, such living systems include not only the simplest organisms, but also higher ones, and even humans.

It is impossible to stop the progress of science/research and technology, as this is a natural process. However, technologies are not alike: some of them have evidently positive social, economic and other effects, while others do not. Most frequently, a new technology has a certain set of positive and negative (undesirable) properties, qualities, and characteristics, which complicates and renders difficult the decision on whether its use and application should be broad or limited. The issue of value-related priorities, of a hierarchy of values for a particular society or state, is becoming increasingly relevant.

Some technologies are intended primarily for specific individual purposes (e.g., medical abortion, surrogacy), some others — for state purposes (e.g., missile, space and other military technologies), and still others — for public, social, purposes (e.g., healthcare or waste disposal technologies).

In our opinion, the cutting-edge technologies should, mostly and primarily, serve not an abstract economy focused on making a profit "at any cost" (to the detriment of public interests, ecology, etc.), but the implementation of such fundamental human values as preserving and maintaining people's health, as well as increasing the duration of their active and healthy life. A high quality of life is possible only if there is affordable and healthy food, clean water and air, comfortable housing, and favorable environment. At the same time, we cannot forget about the limits of economic growth and unequal distribution of wealth, which, on the one hand, require imposing certain restrictions on the traditional (extensively developing) industries and sectors of the economy, and, on the other hand, require stimulating the development of technologies which can ensure the transition from the extensive path of economic development to the intensive one. The issue of environmental sustainability of biosystems is becoming more and more pressing, and a timely settlement thereof is a prerequisite for resolving the accumulated problems of both the functioning economy, and the

emerging bioeconomy fraught with environmental risks incomparably higher than those well known to us.

Advances in technologies require determining the key vectors of development thereof, as well as understanding (at various levels, from researchers in labs and innovative businesspeople to policymakers) the logic of the development of society in the context of a new biological and digital reality.

In this connection, the issues of strategic planning and comprehensive technology assessment come to the fore. It is not a mere coincidence that assessment of cutting-edge biological and other technologies increasingly includes not only the assessment of their effectiveness (by type: economic, medical, social, energy-related, etc.) and safety (social, biological, etc.), but also the ethical and legal assessment, which, in turn, drives further development and institutionalization of bioethics and biolaw as a science, a sphere of applied research, expert practice, emerging regulators of an increasing number of social relations in bioeconomy.

III. Bioethics as a Phenomenon and Its Significance in Regulating the Emerging Bioeconomy

One of the founders of bioethics, Van Rensselaer Potter (2002), outlined the goal of this science: to learn to survive in new conditions, which requires taking into account both the biological knowledge and the universal human values when making the most important decisions.

The subject of bioethics is undergoing the process of crystallization. In simplified terms, bioethics is understood as the science dealing with moral/ethical behavior with regard to life, health, and the attitude of an individual to living things (humans, animals, plants, the environment, the biosphere).

Irina Siluyanova (2008, p. 256) looks at bioethics from the standpoint of its overarching ultimate task — that of preserving the human life.

Natalya Sedova (2005) speaks about the non-formal regulation of relations in medicine and other spheres, distinguishing the theoretical (science and research), practical and applied spheres in it.

Igor Ponkin and Alexandra Ponkina (2014) suggest considering bioethics as a science (studying moral, ethical, legal, and anthropological issues) and a system of regulations (a set of deontological imperatives in medicine, pharmaceutics, etc.).

Noteworthily, the reference to the system of regulations is positive in some definitions, and significant for us.

In Russian science/research and specialist publications, bioethics is closely associated with medical ethics and medical deontology (Semina, 2021). This is due to the developed state of medical ethics, and the legitimization of ethical principles specifically in relation to medicine and healthcare. Ethics-related regulation is also common in the sphere of circulation of pharmaceuticals and medical devices. The Russian legislation contains provisions directly stipulating the activities of ethics boards, councils or committees, and the procedures for ethics reviews with regard to certain medical products requiring official registration before going to market.

In science and research as a whole, as well as in biology, psychology and some other spheres of activity sensitive in terms of ethics, the situation is much worse. These spheres lack not only ethics-related standards and (or) institutions, but sometimes even special industry-specific (or sector-specific) laws which could stipulate and formalize the ethics-related issues.

Bioethics is not a purely corporate entity (like medical ethics, or the ethics of a lawyer, notary, etc.), but functions as a multidisciplinary field of knowledge that establishes, develops and upholds — using its own resources and capabilities — the basic ethical principles regarding its subject matter and area.

A number of countries not only allow for certain elements of institutionalization of bioethics, but have bioethics centers actively functioning on a permanent basis (e.g., Center for Bioethics at the Catholic University of the Sacred Heart (Italy); Institute for Bioethics (Netherlands); Centre for Biomedical Ethics and Law at the University of Louvain (Belgium)).

In Russia, there are ethics (bioethics) boards/councils (committees) affiliated with the Ministry of Health of the Russian Federation, as well as local ethics boards/councils (committees) affiliated with medical

and some research organizations. However, a clear understanding of their structure, principles, subject matter, operational boundaries, and hierarchy, has not formed yet. In recent years, due to the development of genetic, information and other technologies, the interest in bioethics, as well as in bioethics boards/councils (committees) and other institutions, has increased. There are proposals to create a developed network of such institutions, and to ensure implementation of a single national policy in this area, in the way similar to some other countries (Mokhov, 2020).

Despite the differences in approaches to defining the subject matter of bioethics, as well as its boundaries, the correlation of spheres, and the importance of science/research and practice in bioethics, most authors point out that one of the tasks of bioethics is to establish some standards and guidelines. At the same time, the authors' positions may differ: from complete absorption of law by bioethics to an almost complete or partial demarcation between the norms of ethics and law, the ethical and the legal regulation of the most important kinds of relations (from conception of life to death and even further).

In our opinion, the truth is between the two extremes. The norms (standards) of professional ethics and ethics in general have existed and, apparently, will continue to exist for a long time. As a rule, with the development of the state, law and legislation, they tend to increasingly play not a decisive, but an important auxiliary role in the regulation of certain kinds of social relations (professional, employment, etc.) in the boundary zones where, on the one hand, regulation is necessary, and, on the other hand, "non-legislative" regulation is considered to be acceptable and sufficient at a certain stage of the state, law, and society development. All of the known legal norms were once moral, ethical, or religious norms, but not all of the known social norms — for various reasons (from insufficient significance, or the limits to which law can intervene in certain relations, to the impossibility of an accurate description) — become legal norms. Moreover, a direct conflict is possible between some of them, which is resolved in favor of the legal norm as a definite and formalized gauge of what is considered to be right.

At the same time, ethics and the norms thereof, although conventionally considered to be auxiliary regulators, to be standard,

generally accepted, non-legislative rules, are no less important, and sometimes — at a certain stage of society, law and legislation development — are the only regulators of social relations. Nowadays, they even might be considered a "new religion" during formation and development of biotechnological and digital reality, in a rapidly changing global landscape. They reflect the foundations, the bonds of society, based on the norms of morality, religion, traditional culture, and the experience of past generations.

The existing differences between law and ethics (bioethics) allow bringing up and discussing the issue of biolaw as another regulator of bioeconomy.

IV. Biolaw as a Phenomenon and Its Significance in Regulating the Emerging Bioeconomy

The debate about the place of ethical norms in the system of social regulators, the existence of similarities with and some fundamental differences from the norms of law, including a common subject-matter domain and non-coinciding areas, the correlation and the boundaries between governmental regulation and self-regulation, as well as "hard" and "soft" regulation, allow speaking about biolaw along with the phenomenon of bioethics.

In specialist publications, the following common features of ethical and legal regulators are usually mentioned: they are social norms; they are obligatory for those to whom they apply; there are sanctions for their violation (Valiev, 2016); the norms are of a practical, applied nature (Bakshtanovskii and Sogomonov, 2007).

The main differences between ethical and legal norms are as follows: wider boundaries of ethics in comparison with law (law is a minimum of ethics (Gutnik, 2017)); a legal norm comes from the government, while an ethical norm comes from the professional community; the procedure, the process for adopting and communicating a legal norm is strictly defined by law, which is not the case with ethical norms (they are adopted based on the established rules, and customs; although adoption of some ethical norms is sanctioned by law or in accordance with the procedure established by law); a norm of law is a form of governmental

regulation, while the norm of ethics is a form of self-regulation, self-organization of the type or the sphere of professional activity; the subsidiary role of ethical norms in regulation of certain social relations.

As Sergey Alekseev (1966) point out, law is the main instrument of the state through which social relations are influenced in order to organize them. In certain instances, the borderline between a norm of bioethics and a norm of law (legislation) becomes completely or partially erased (from "soft law" to direct implementation of an ethical norm into a norm of law).

For example, in Russia, the ethical principle of confidentiality, medical (health) privacy, is also a legal principle formalized in Article 4 and some other articles of Federal Law No 323-FZ [in Russian: № 323-ФЗ] of 21 November 2011 entitled *Fundamentals of Public Healthcare in the Russian Federation*.[2]

The need to protect vulnerable people has been reflected both in Federal Law No 323-FZ of 21 November 2011 (Fundamentals of Public Healthcare in the Russian Federation), and in Federal Law No 61-FZ [in Russian: № 61-ФЗ] of 12 April 2010 (*Circulation of Pharmaceuticals*),[3] as well as in other federal laws and regulations.

Of interest is the experience of other countries with a practice of formalizing ethical norms in legislation through which many ethical norms become legal norms. However, in such instances, ethical regulation remains in place, and the work of ethics boards/councils (committees) acquires a new ethical and legal meaning, despite the significant differences in assessing the issues of bioethics in different countries (Zakharova, 2020).

For example, in France, the Bioethics Law has been adopted and — with some amendments — has been in effect for more than two decades.[4] South Korea has the Bioethics and Safety Act[5] in place. The Chinese

[2] Collection of Legislation of the Russian Federation, 2011, No 48, Art. 6724.

[3] Collection of Legislation of the Russian Federation, 2010, No 16, Art. 1815.

[4] Projet de Loi relatif à la bioéthique. Available at: https://www.assemblee-nationale.fr/dyn/15/textes/l15t0474_texte-adopte-seance.pdf [Accessed 24.12.2020]. (In Fr.).

[5] Bioethics and Safety Act. Available at: https://mbbnet.ahc.umn.edu/scmap/KoreanBioethics.pdf [Accessed 24.12.2020]. (In Eng.).

Biosecurity Law[6] includes the norms regulating research in the sphere of biotechnologies in order to prevent any kind of misuse thereof.

Biolaw is usually mentioned in Russian research papers and publications without an analysis of its essence, subject matter, or other features. In its most general form, biolaw makes it possible, with sufficient degree of completeness and certainty, to perform systemic regulation of the key social relations arising in various spheres of economy (medicine, pharmaceutics, industry, agriculture, energy sector, etc.) in connection with development, creation, implementation, and application of cutting-edge biotechnologies.

Biolaw is a phenomenon that has not gained sufficient attention in the Russian science of law yet. It emerged at the junction and almost simultaneously with bioethics, but it cannot be reduced to bioethics only, since legal norms — unlike ethical, moral, or other kinds of norms — are obligatory for everyone and formally defined. A thing that bioethics and biolaw have in common is the platform: the human activities involving the use of living matter (Luk'yanov, 2008) to accomplish a fairly wide range of tasks. Partially, the range of tasks facing biolaw is accomplished within the framework of the science of medical, environmental and some other branches of law, the subject matter of which is narrower as compared to bio-law (the sector-based, or the activity-based approach).

In our opinion, biolaw can be understood as a totality of various kinds of social relations (from use and preservation of the animal world to biomedical, biopharmaceutical, bioenergetic and other types of activities), where biotechnologies, biosystems, cells, tissues, or organs of plants, animals and humans are used.

Biolaw is not a separate branch of law either in terms of the scale of the tasks to be accomplished, or in terms of the area of application, or in terms of the range of entities the activities of which are subject to legal regulation. We are talking about supra-sectoral regulation of social relations that have a common technological platform, as well as common foundations and principles.

[6] Biosecurity Law of the P.R.C. (中华人民共和国生物安全法). Available at: https://www.chinalawtranslate.com/en/biosecurity-law/ [Accessed 24.12.2020]. (In Eng.).

In connection with the above, biolaw has a complex structure of internal (within the boundaries of law) and external relations (with other spheres of practice, and areas of human knowledge). It actively uses the experience/practices of the theory of law and state, administrative and civil law, as well as medical, pharmaceutical, sports, environmental, energy and other branches of law (legislation).

The development of bioeconomy and the individual spheres thereof requires prompt development of this branch of science, at least for the sake of ensuring efficient law-making and expert work. In the absence of such development, noticeable difficulties are already arising in practice with the development and implementation of genetic and other technologies, biomedicine and biopharmaceutics, biobanking, etc.

V. Conclusion

Advances in technologies require determining the main vectors of their development, as well as understanding — at various levels — of the inner logic of their development, which, in the present-day law-governed and welfare states, is unthinkable without an ethical and legal base.

In practical terms, bioethics is a system of standard, generally accepted, non-legislative rules. In certain individual instances, the borderline between a norm of bioethics and a norm of law (legislation) becomes completely or partially erased (from "soft law" to the direct implementation of an ethical norm into a norm of law).

Biolaw emerged at the junction with bioethics, but cannot be reduced to bioethics only, since most of the legal norms are obligatory for everyone and formally defined. It has complex connections and correlations with bioethics, having a common subject-matter domain with bioethics, but not absorbed by the latter.

Bioethics and biolaw provide an ethical and legal framework for relevant (legitimate) activities aimed at the development of bioeconomy as a whole, as well as individual spheres and sectors thereof.

Bioethics and biolaw are making their first steps in Russia. The development of legislation in this area, building on the existing experience and practices of law, ethics and other sciences, will become one of the drivers of bioeconomy development in Russia.

References

1. Alekseev, S., (1966). *The Mechanism of Legal Regulation in a Socialist State*. Yuridicheskaya literatura, p. 187. (In Russ.).

2. Bakshtanovskii, V. and Sogomonov, I., (2007). Applied Ethics: Idea, Foundation, Way of Existence. *Voprosy filosofii*, 9, pp. 45–48. (In Russ.).

3. Bbsrc.ukri.org. (2015). BBSRC, Biotech Britain. [online] Available at: https://bbsrc.ukri.org/documents/capital-economics-biotech-britain-july-2015/ [Accessed 10.12.2020].

4. BECOTEPS. The European Bioeconomy in 2030 — Delivering Sustainable Growth by addressing the Grand Societal Challenges. (n.d.). [ebook] Available at: http://www.plantetp.org/images/stories/stories/documents_pdf/brochure_web.pdf [Accessed 10.12.2020].

5. Brunori, G., (2013). Biomass, Biovalue and Sustainability: Some Thoughts on the Definition of the Bioeconomy. *EuroChoices*, 12(1), pp. 48–52.

6. Gutnik, O., (2017). The Institute of the Independence of the Court in Criminal Proceedings in the Russian Federation. *Lex russica*, 4, pp. 67–73. (In Russ.).

7. Ivashkovsky, S., (2011). Economy and Ethics: the History of Difficult Relations. *Ekonomicheskaya politika*, 3, pp. 114–141. (In Russ.).

8. Luk'yanov, A., (2008). *Bioethics with Basics of Biolaw*. Moscow: Nauchnyy mir. (In Russ.).

9. Mateescu, I., Popescu, S., Paun, L., Roata, G., Bancila, A. and Oancea, A., (2011). Bioeconomy. What is bioeconomy? How will bioeconomy develop the next two decades. *Studia Universitatis «Vasile Goldiş», Seria Ştiinţele Vieţii*, 21, pp. 451–456. (In Eng.).

10. Mokhov, A., (2020). The Concept of Four "Bios" in Law and Legislation. *Aktualnye problemy rossiiskogo prava*, 15(8), pp. 146–154. (In Russ.).

11. Mokhov, A., (2020). The Council of the President of the Russian Federation on Ethics. *Aktualnye problemy rossiiskogo prava*, 15(12), pp. 23–31. (In Russ.).

12. Ponkin, I. and Ponkina, A., (2014). Bioethics as a science and as a lex biomedica. *Pravo i obrazovanie*, 7, pp. 80–93. (In Russ.).

13. Potter, V., (2002). *Bioethics: Bridge to the Future*. Kiev: Vadim Karpenko. (In Russ.).

14. Schwab, K., (2016). *The Fourth Industrial Revolution*. Moscow: Eksmo, p. 138. (In Russ.).

15. Sedova, N., (2005). The Legal Status of Bioethics in Present-Day Russia. *Medical Law*, 1, pp. 11–15. (In Russ.).

16. Semina, T., (2021). *Medical Ethics: Bioethics — the Path to the Future*. Moscow: Kanon, ROOI «Reabilitatsiya», p. 240. (In Russ.).

17. Siluyanova, I., (2008). *The Chosen Ones. The Vocation of a Medical Practitioner*. Moscow: Forma T, p. 256. (In Russ.).

18. Valiev, R., (2016). The Legal Nature and Classification Identity of the Norms of Law Enforcement Ethics. *Russian Law Journal*, 5, pp. 19–28. (In Russ.).

19. Zakharova, M.V., (2020). The Rosie effect or the dialectics of the social and the biological in the evolution of the legal map of the world in the 21st century. *Courier of Kutafin Moscow State Law University (MSAL)*, 4, pp. 50–56. (In Russ.).

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Bioethical Aspects of Human Rights in Modern Latin America

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Abstract: The aim of the paper is to analyze the bioethical aspects of the institution of human rights in Latin America. The result of the present research is the author's conclusion on the necessity of the practical implementation of legal provisions in this area, and their judicial enforcement in many states of Latin America with the aim of compliance with international standards of human rights. In the face of global uncertainty of COVID-19, it is more necessary than ever to maintain a strong commitment to international law and human rights with responsibility in bioethics, and also to seek to preserve and consolidate what has been advanced in the construction of a world order based on rules and shared values, along with a policy structured on common values and international principles. States must take international responsibility for wrongful acts for the violation of human rights in biolaw. The research methodology was based on general scientific and private scientific methods of cognition (the dialectical method, methods of analysis and synthesis, deduction and induction, comparative legal and historical legal methods). The biolaw basing on the International Law and Human Rights has its special understanding of the issue, which should be supported by further legislative development in Latin America. Latin American courts will not be able to make judgments on bioethical issues for a long time, while it is closely related to biopolitics and other controversial regional political positions. There are structural and historical problems of Latin American legal culture, a high index

of criminal impunity and wide discretion of law-enforcement agencies that do not apply specific principles of biolaw and even bypass official bioethical guidelines in their practice. The author's give overview of the practice of Mexico on the matter of the legislative process in biolaw. The paper focuses on different theoretical approaches.

Keywords: bioethics, biopolitics, biomedical technologies, biolaw, genetics, human rights, justice, patient rights, legal culture, COVID-19

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Contents

I. Introduction

Law, just like social sciences and arts, is always observing the world and people. It is not a simple observation. It is a complex vision through social sciences, arts, and law altogether. This vision is not just complex, it is stereoscopic and scattered like a light reflected by a prism (Cárdenas Quiroga et al., 2015).

The vision sometimes gets transformed because the light or perspective is constantly changing. This is what happens when we look at ourselves in mirrors and the key thing is the image it reflects or the riddle it gives. Although sometimes the best vision of us is through the eyes of our friends. But the issue is that law and all other disciplines are guidelines, which, when synchronized, allow us to evaluate various things around. That is why, by looking at bioethics, we place ourselves in the company of lawyers who come along with us on this trip.

Currently, bioethics is a rapidly developing interdisciplinary sphere in Latin America. Being a special branch of science and practical

activity, bioethics differs from biopolitics (Denisenko and Trikoz, 2020). But bioethics is still not much influential in the Latin American region from the academic point of view. On the whole, bioethical programs are supported only in big cities and only in some countries (Álvarez-Díaz, 2012).

The Black Swan of COVID-19 unexpectedly changed the whole perception of the facts (Malinovsky, Osina and Trikoz, 2021). Recently, *The New York Times* published the statistics of people killed by COVID-19 and the statistics of the unemployed in the US. The optimism was ruined by reality, as usual.

That is the reason why sometimes lawyers seem bureaucratized intellectuals who are far from the reality that motivates us. The idea that we have in mind is the urgent need for the law to have done what must be done in the fight for bioethics as well as to combat climate change and other contemporary challenges. We know that it is a voice crying in the wilderness of existing rules.

According to the National Commission of Bioethics in Mexico (La Comisión Nacional de Bioética — CONBIOÉTICA), 'bioethics is a branch of applied ethics, which reflects, examines, and applies normative and socio-political approaches to managing and resolving conflicts in social life, especially in life sciences, medical practice, and medical studies, which affect life on the planet both now and in the future'.

This definition of bioethics is typical of the Latin American region and it stems from the necessity to develop a conceptual approach since a generally accepted definition of bioethics has not been framed yet. The term bioethics was introduced almost a hundred years ago. In 1927, *Fritz Jahr* defined bioethics as the ethics of the way people deal with animals and nature. But it was Van Rensselaer Potter who brought the term into the modern scientific discourse in his article *Bioethics, the Science of Survival* (1970).

II. The Complex Latin American Model of Bioethics

Bearing in mind that the law is in a position to take responsibility for human well-being, let us see how the combination of international law and human rights can operate in the contemporary world where

forests are burning, the pandemic is booming, and many conflicts remain unsolved.

First, it is difficult to synthesize the objective expressions of international law and human rights as well as their conceptual frameworks. Anyway, we are going to see whether the previous problems and concerns will dissipate, for example, smoke after fires or ill health after vaccinations.

All the events that frame international crises, generally with serious violations of human rights, make us address to other disciplines, which are related to jurisprudence. *Bioethics* is understood as a branch of ethics dedicated to promoting the principles for the most appropriate conduct of human beings with respect to human life and the life of other living beings as well as the environment with acceptable conditions to make all these achievements possible.

Nowadays, bioethics is 'an ongoing interdisciplinary life science dialogue through the lenses of human values aimed to frame, express, and probably solve a number of problems, arising in the process of laboratory research, intervention in human life, environment, and the Earth's biosphere'[1]. This detailed definition is used by the Regional Office of Bioethics under the Pan American Health Organization (Santiago de Chile). In legal discourse, bioethics implies a philosophical, moral, and ethical evaluation of medico-biological procedures, studies, treatment methods, genetic engineering technologies, organ transplantations, caring for terminally ill people, etc. (Stepke, 2010). In the Latin American region, bioethics is regarded in close relationship with the tools for human rights protection, promotion of democracy, and civic engagement. It results in a more politicized concept of bioethics (Cossio, 2013).

According to Vila-Coro Barrachina, it is possible to distinguish three types of bioethics, depending on the way it is applied: a) conceptual (theoretical) bioethics or 'meta-bioethics' as a science; b) cultural bioethics, aimed to raise new bioethical dilemmas in historical and socio-

[1] Selecciones de Bioética No 15 del Instituto de Bioética de la Pontificia Universidad Javeriana de Colombia. Archivado desde el original el 5 de junio de 2016.

cultural contexts; c) clinical bioethics (medical deontology), proposing ethical solutions for the problems, which arise in the professional treatment of patients; d) normative bioethics (*biolaw*) (Garcia et al., 2019; Trikoz, 2020), embracing healthcare rules of law, which come from lawyers and public authorities (Vila-Coro Barrachina, 2010).

In 1979, Tom L. Beauchamp and James F. Childress published the book *Principles of Biomedical Ethics*. The book has become a doctrinal landmark. It is still commonly cited because it contains arguments for the *classical triad of bioethical principles*: beneficence, nonmaleficence, autonomy, and justice. These principles are closely related to the concepts of *respect for human dignity, human rights and autonomy protection, tolerance, inclusiveness, solidarity, and non-discrimination*. These are the guidelines for the practical application of bioethics in the Latin American context.[2]

Inequality is an undeniable fact in Latin America. This fact is underlying two bioethical premises — the pursuit of justice and protection for everybody. A special historical context of Latin American bioethics builds on the regional cultures and their links to Anglo-Saxon, Portuguese, Spanish, and Mediterranean traditions. In the beginning, it was a combustible combination of the despotic ethics, typical of colonial conquest times, and the paternalistic ethics of the colonial domination and caste system. But paternalistic treatment in medicine and bioethics never reached the lowest level of the Latin American caste system (Guerra, 1972). In the modern era, the development of Latin American bioethics resulted in ethnical independence and bioethical sovereignty with new principles: the institutionalization of local bioethics committees; informed consent; autonomy of the patient; consultations on ethical and legal issues; obligatory prenatal diagnostic tests; availability of reproductive technologies; bioethics of cell, tissue, and organ transplantations; controlled genomic experiments, etc. Nevertheless, three main goals of bioethical studies have not been achieved yet: education and enlightenment, public health, and political influence (Mainetti, 1998).

[2] ¿Qué es Bioética? Available at: http://www.conbioetica-mexico.salud.gob.mx/interior/queeslabioetica.html [Accessed 24.01.2021].

Alfonso L. Escobar notes that culturally and technologically Latin American countries are not yet ready for the humanization of advanced biotechnologies because they are still strongly influenced by catholic ethics, conservative Hippocratian tradition, and paternalistic ideology (Escobar, 2010). An opposite opinion is put forward in another expert publication by Edmundo Estévez and Agustín García. It is a work on ethical and legal issues of future medicine, human genome studies, the right to abortion, the rights of unborn children, ethical treatment of animals, etc. (Estévez and García, 2009).[3]

Currently, Latin American legislative initiatives and studies of relationships among bioethics, theology, medicine, and law are booming. This fact is within the overall trends of bioethics. The urge in bioethical studies was facilitated by FELAIBE, the Regional Program on Bioethics under the Pan American Health Organization, the Center of Bioethics at the San Paolo Bolivian Catholic University, the Latin American and Caribbean Congress of REDBIOÉTICA, and Human Genome Meeting in Cancún (Mexico). In 2010, an international conference, organized by UNESCO in Mexico City, brought together the representatives of Latin American bioethics bodies and the European Commission. They met to share experiences in fulfilling national obligations, including obligations on *the Universal Declaration on Bioethics and Human Rights of 2005*.[4]

Recently, the problems of the legal status of unborn children and the protection of an embryo's rights have become topical in the region. The Western European legal tradition is very influential in this area. It sets the framework for regulation by analogy with the solution of the issue, provided by the rules of the biolaw and case law of the European Union (Gulyaeva and Trikoz, 2018; 2020). The trend is facilitated by the rapid development of modern molecular genetic diagnostics methods in the

[3] Latin American and Caribbean Federation of Institutions of Bioethics (Federación Latinoamericana y del Caribe de Instituciones de Bioética). Available at: http://www.felaibe.org [Accessed 24.01.2021]; REDBIOÉTICA has its own Web portal, with an Analysis Department based in Buenos Aires, (www.redbioeticaunesco.org) and the online publication of REDBIOÉTICA UNESCO Journal [Accessed 24.01.2021].

[4] Bioethics Committees reached an agreement on their work in Mexico. UNESCO Social and Human Sciences Sector magazine. January-March 2010. 3.

EU and North America. One of the topics of the 6th Framework Program on EU Research was about the ethical and legal considerations on the possibility of a) carrying out scientific research on human embryos on national territories; b) carrying out scientific research on stem cells derived from human embryos after the 6th Framework Program on EU Research is launched; c) producing stem cells by deriving them from human embryos.

The European Parliament expressed its opinions in three principal resolutions: the first resolution (1989) on genetic engineering invites all the Member States to forbid, by virtue of specific legislative provisions, any gene transfer to human germ line cells; the second provision (1989) on artificial insemination both in vitro and in vivo is particularly rigorous about research activities on embryos; the third resolution (1997) concerns a total ban on human beings cloning. In 1998, the European Group on Ethics and Science in New Technologies decided to deprive research projects, which resulted in the destruction of human embryos, of community funding.

Among the Member States, there is an agreed consensus on when scientific research on embryos is allowed. The ECHR Member States are entitled to exercise broad discretion in terms of enacting the legal regime to be applied to the donation of embryos.[5] Embryos are protected under the laws of other legal systems of the European Union (Pardinini, 2004). Every human being shall have the right to life and human dignity; the life of a fetus shall be protected from the moment of conception (Vincze and Varju, 2012). For example, in Italy, interventions are permissible only to guarantee the embryo's integrity and for its recovery, avoiding disproportionate risks. Indeed, carrying out scientific research on an embryo is a complex issue (especially when evaluating the potential risk of its destruction). The Law on Medically Assisted Procreation of 2004 not by chance emphasizes the 'right of the conceived to a certain identity as well as to a non-manipulated genetic heritage'. But the Law simplifies the issue related to the destiny of supernumerary embryos by highlighting that 'the issue shall not be addressed through a general law on medically assisted procreation'.

[5] para. 183 of the Parrillo decision. ECHR 27 August 2015, Parrillo v. Italy.

More Latin American laboratories are adopting the methods of reproductive medicine genetic diagnoses: pre-implantation genetic diagnosis and prenatal testing. Some Latin American countries still do not have any legal prohibitions or restrictions on such diagnoses. That is why it is up to the managers of private clinics and genetic research labs to decide how much this or that procedure is appropriate and ethical. Moreover, there are problems with independent licensing and legal regulation of these activities. There are not so many well-prepared certified geneticists. Human dignity can, beyond its ontological and constitutional value, constitute a legal limit for scientific manipulations with human embryos in accordance with moral principles and respect for human life.

III. Can Bioethics Show a Better Future in Latin America?

The truth is that bioethics is now responding to the 21st century crisis of the techno-scientific era. This crisis is both vital and normative. It is about threatened life and broken morality. They provoke three main factors: the environmental catastrophe, the biological revolution, and the medicalization of culture. As Mainetti (1998) asserts, there has been a shift in cultural paradigms.

In the same way, *bioethics*, i.e. the paradigm of techno-scientific ethics, provides us with a technological imperative according to which everything that can be done must be done. Halfway between the apocalyptic forecasts and messianic prophecies of techno-science, there is the third facet of the *universal bioethical paradigm*, which affirms humanism and proclaims the principles of autonomy, beneficence, freedom, and well-being of a moral and reasonable person.

Thus, the light at the end of the tunnel seems to be a way out but along the way, we will have to go through the succession of symbolic tunnels. These are the tunnels of reproductive ethics, which requires analyzing the issues of contraception, sterilization, and abortion alongside with studying the relationships between life expectancy and the quality of life. Mainetti also touches upon a complex morality of

assisted reproduction that provokes so far, a peaceful controversy between Catholics and secularists. The need for legal regulation on the matter is becoming more urgent every day. The same is also true for thanatological ethics, the ethics of death, the ethics of research, and the ethics of health.

Environmental ethics must also be taken into account (Malinovsky, Osina and Trikoz, 2020). Perhaps bioethics will be a new chapter in the book of human rights for the next millennium. Bioethics will become a part of the new rights because if development consists of health, well-being, and progress, health is going to mean the quality of life and progress is going to mean sustainable development.

We are planning what bioethics should be at the time of COVID-19, feeling a big discomfort, which requires insisting on the ethics of the common good and just society. It is a kind of macro ethics, which aims at the consolidation of civil and political rights as well as making economic, social, and cultural rights available to everybody.

It seems that the tunnels lead us to the Socratic classicism. Borges and Socrates are lighting the way out of the mirrors and the tunnels. The door opens for us to ponder ethics, history, and human rights framed in a new law. We should not use the words *escape* or *exit*. In Latin, the word *exitus* also meant *success, result,* or *end*. A very common phrase was *incerto exitu victoriae* — the result of the victory is uncertain. Thus, the word *success* probably matches the situation well.

In Latin American countries, all human rights are developing but actually only one human right is possible — the one that ensures the dignity of people.

In the early 2000s, Latin American countries started a new cycle of the legal regulation of bioethics, clinical practices, and genetic studies (Bulle Goyri, 2013). In Brazil and later in some other countries, the right to a decent standard of living and access to medical care was fixed constitutionally. In the context of bioethics, this right is regarded as a universal right of working people (Garrafa, Rocha da Cunha and Manchola, 2018).

Mexico has established a National Commission on Bioethics (CONBIOÉTICA), which has become the main centralized body of the

Health Ministry. CONBIOÉTICA is a technically and organizationally autonomous unit. It is responsible for setting up national policy and legislative proposals in the field of bioethics. It supported the adoption of the *Mexican Healthcare Law* of 2009 and the *Agreement by Consejo de Salubridad General* of 2014, which established a program to improve the life of terminally ill patients (Hall, Campos Pacheco and Pérez Audiffred, n.d.). The Mexican Bill of Rights of Patients, first introduced in Parliament in 2001, is being debated for over 20 years. There is a proposal to fix a patient's right to consent to treatment or refuse from it. CONBIOÉTICA emphasizes that very often medical practitioners are not aware of a patient's right to refuse from treatment. That is why doctors seldom discuss treatment options with their patients and this fact contradicts the bioethical principle of informed consent (Camino and Hall, 2020). Under the Criminal Code of the Mexican state of Querétaro, a doctor who has violated ethical principles in medicine can be sentenced up to three years of imprisonment.[6] Another Mexican state of Tabasco has a Law on Assistive Reproductive Methods, which adds contractual surrogacy rules to the Civil Code of the state (Camino and Hall, 2020).

It should be noted that the *Ethics Code*, applicable to the Mexican federal public servants, contains the principles, which the public servants must follow. Among them, there is *a principle of equality and non-discrimination*. The public servants are working for everybody without any exception, i.e. regardless of an ethnic or national origin, skin color, culture, sex, age, or disability; social, economical, medical, or legal status; pregnancy, language, belief, sexual orientation, personal or political preferences; marital status, criminal record, or any other reason.[7] This provision meets modern international standards in the

[6] Poder Legislativo del Estado de Queretaro (2009) Codigo Penal para el Estado de Querétaro, Article 243. LVIII Legislatura Queretaro. Direccion de Investigacion y Estadistica Legislativa. Available at: http://legislaturaqueretaro.gob.mx/app/uploads/2016/01/COD004.pdf [Accessed 24.01.2021].

[7] Código de Ética de los Servidores Públicos del Gobierno Federal [Accessed 24.01.2021].

sphere of human rights at the time of the fourth industrial revolution. On the whole, Mexican law is an example of a well-developed legislation on the issues of bioethics, genome studies, and other aspects of the emerging branch of *biolaw*.

IV. Conclusion

Indeed, the humanism of the 20th century, which people used as the measure of all things and an epistemological basis, can no longer be adapted to the new information societies, which are rather speedy, scientific, and technological.

To escape from that standard, it is necessary to pass a law that would make people do what needs to be done while fighting for the survival of the planet. The author of *Sapiens: a Brief History of Humankind* and *Homo Deus: A Brief History of Tomorrow* affirms that now we have three enemies that threaten all humans. Their threats should make us work together. These enemies are nuclear war, climate change, and technological disruption. All of these are global enemies, which cannot be defeated by any particular nation. We recognize the existence of transnational actors but in this situation, it is necessary to work much and consolidate the efforts of both international agreements and international organizations. They should operate in a transparent and active network, protecting human rights. The other alternative consists of perceiving history in its entirety and striving to unravel the mechanisms of the future, with an accurate determination about the destiny of international law and human rights in the context of bioethics.

In the face of global uncertainty, it is more necessary than ever to maintain a strong commitment to international law and human rights, covered with responsible bioethics. At the same time, there are serious problems that can hinder legal provisions on bioethics from practical implementation. For instance, J.R. Cossio, an ex-justice of the Mexican Supreme Court, cited the case, challenging the law that decriminalized abortions in Mexico City. He believes that Latin American courts will not be able to pass landmark judgments on bioethical issues until they are bound by biopolitics and other controversial political positions (Cossio, 2013).

Mexico shares this trend with many Latin American countries. It happens due to many factors, including structural and historically entrenched problems of the Latin American legal culture, e.g. the high level of criminal impunity and wide discretion in law enforcement. As a result, specific principles of the biolaw and official bioethical recommendations are easy to circumvent.

References

1. Álvarez-Díaz, J.A., (2012). Bioética latinoamericana o bioética en Latinoamérica [Latin American bioethics or bioethics in Latin America]. *Revista Latinoamericana de Bioética*, 1, pp. 10–27.

2. Bulle Goyri, V.M., (2013). *Bioética, Derecho y Derechos Humanos. Perspectivas de Bioética*. Mexico.

3. Camino, B.G. and Hall, R.T., (2020). Bioethics and the Law in Mexico. *Rev Bio y Der*, 49, pp. 107–123.

4. Cárdenas Quiroga, E.A., Morales Martín, L.Y. and Ussa Caycedo. A., (2015). La estereoscopía, métodos y aplicaciones en diferentes áreas del conocimiento. *Rev. Cient. Gen. José María Córdova,* 13(16), pp. 201–219.

5. Cossio, J.R., (2013). Derecho y Bioética. In: González Valenzuela J. (ed). *Perspectivas de Bioética*. Mexico: University Nacional Autónoma de Mexico.

6. Cossio, J.R., (2013). *Derecho y Bioética. Perspectivas de Bioética*. Mexico: University Nacional Autónoma de Mexico, Comisión Nacional de los Derechos Humanos and Fondo de Cultura Económica.

7. Denisenko, V. and Trikoz, E., (2020). Biopolitics and legal issues of emergencies in the context of coronavirus pandemic. *E3S Web of Conferences*, 175(14013), pp. 1–7, doi: https://doi.org/10.1051/e3sconf/202017514013. (In Russ.).

8. Escobar, A.L., (2010). Bioethics in Latin America and Colombia. In: *Ibero-American Bioethics: History and Perspectives*. Springer Science.

9. Estévez, E., and García, A., (2009). *Bioética de intervención. Los derechos humanos y la dignidad humana*. Quito: Textos de enseñanza universitaria.

10. Garcia, L.F., Fernandes, M.S., Moreno, J.D. and Goldim, J.R., (2019). Mapping Bioethics in Latin America: History, Theoretical Models, and Scientific Output. *Journal of Bioethical Inquiry*, 16(3), pp. 323–331.

11. Garrafa, V., Rocha da Cunha, T. and Manchola, C., (2018). Access to Healthcare: A Central Question within Brazilian Bioethics. *Cambridge Quarterly of Healthcare Ethics*, 27(03), pp. 431–439.

12. Guerra, F., (1972). Medicina colonial en Hispanoamerica. In: Entralgo, P. Lain (ed). *Historia universal de la medicina*. Salvat, Barcelona.

13. Gulyaeva, E.E. and Trikoz, E.N., (2020). Legal Aspects of Bioethics and Genomics in Latin America. *Aktualnye problemy sravnitelnogo prava*, 1, pp. 42–49. (In Russ.).

14. Hall, R.T., Campos Pacheco, E.G. and Pérez Audiffred, A.P., (n.d.). Cuidado paliativo: Bioética y la ley lo que opinaron los medicos. *Newsletter, Gaceta of the National Bioethics Commission CONBIOETICA*. Gaceta VI (25), pp. 14–20.

15. Halliday, S.A., (2004). Comparative Approach to the Regulation of Human Embryonic Stem Cell Research in Europe. *Medical Law Review*, 12, pp. 40–43.

16. Mainetti, A., (1998). Bioethics in Latin America. In: Reich W. (ed). *Encyclopedia of bioethics*. London.

17. Malinovsky, A., Osina, D. and Trikoz, E., (2020). Legal Instruments for Stimulating Environmentally Friendly Behavior: Successful Practices in Russia and Abroad. *E3S Web of Conferences,* 164(11039), pp. 1–11. (In Russ.).

18. Malinovsky, A.A., Osina, D.M. and Trikoz, E.N., (2021). State Support for the Russian Economy Affected by COVID-19 Consequences (Legal Aspects). In: Ashmarina, S., Mantulenko, V. and Vochozka, M. (eds). *Engineering Economics: Decisions and Solutions from Eurasian Perspective, 139 Engineering Economics Week 2020*. Lecture Notes in Networks and Systems, pp. 283–287, doi: https://doi.org/10.1007/978-3-030-53277-2_33. (In Russ.).

19. Pardini, C., (2016). *Libertà di ricerca scientifica e tutela dell'embrione*. Nuova Giurisprudenza Civile Commentata.

20. Stepke, F.L., (2010). The Pan American Health Organization and Latin American Bioethics. In: Pessini, L., Barchifontaine, Ch.P. de and Stepke, F.L. (eds). *Ibero-American Bioethics: History and Perspectives*. Springer Science+ Business Media B.V.

21. Trikoz, E.N. and Gulyaeva, E.E., (2018). ECHR Positions on Certain Issues of Bioethics and Genetic Data, Advances in Law Studies. *Scientific and Theoretic Journal*, 6(4), pp. 36–40. (In Russ.).

22. Trikoz, E.N., (2020). Communicative Function of Biolaw Development. In: *Legal Communication between State and Society: Domestic and Foreign Experience*. Voronezh. (In Russ.).

23. Vila-Coro Barrachina, M.D., (2010). *La vida humana en la encrucijada. Pensar la bioética*. Madrid: Ediciones Encuentro.

24. Vincze, A., Varju, M., (2012). *Hungary. The New Fundamental Law*. European public law, p. 444.

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Historical Approaches to Euthanasia: the Unfinished Story of a Concept

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Abstract: Various ethics committees in Belgium, Canada, Denmark, Luxembourg, Portugal, and France have made attempts to describe the notion of euthanasia. Opinion No 063 (January 27, 2000) of the National Advisory Committee on Ethics shows that there has been no consensus on the definition of this concept. It is therefore necessary to review historical background of euthanasia from ancient times to modern period to better understand its potential applications in divergent contexts.

Studies devoted to euthanasia usually involve two modalities, namely active and passive. The active modality entails the act of deliberately killing a patient with or against their will in order to relieve persistent suffering, while the passive modality deals with the rational valid refusal of life-sustaining medical interventions necessary for the patient's life and health. The goal of this article is to present different historical approaches to euthanasia from two modalities and engage the bioethics community in a discussion on legal, social, and ethical issues of euthanasia all over the world.

Keywords: euthanasia, assisted dying, ethics, eugenics, hygenists, law

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Contents

1. Introduction

Defining euthanasia is far from being an easy task.

To date, no consensus has been reached around the concept of euthanasia, including among those who agree that it's not the disguised elimination of "undesirables".

Opinion No 063 (January 27, 2000) of the National Advisory Committee on Ethics is the best illustration of this lack of consensus. In their opinion, the definitions of euthanasia proposed by various similar committees (Belgian, Canadian, Danish, Luxembourg and Portuguese) are listed in the appendix. Although they mention and state in a fairly recurring manner an identical syntax and terminology, these definitions diverge in practically every respect and do not suggest any restraint of a common template.

2. A Philosophical History of Euthanasia

The historical study of euthanasia practice demonstrates four different significations to euthanasia: the gentle death; the compassionate euthanasia; the utilitarianist and eugenistic euthanasia.

2.1. The Discipline of Gentle Death

2.1.1. Ancient Times

During this period, several concepts overlap and become intertwined according to collective or individual principles. Euthanasia was a practice that responded to the desire for a beautiful death, a gentle

death or a suicide. The Greek poet Cratinos (5th century BC) used the word euthanatôs to designate both a beautiful death and a gentle death. For Posidippus (c. 300 B.C.), euthanasia expressed both the practice of a good death and a sweet death: man "desires nothing better than a sweet death" (Fragment 16). More contemporary, Suetonius[1] traces the end of the life of Emperor Augustus. In his narrative, he describes him embraced by the arms of Livia, taking advantage of a euthanasia (quick death without suffering) which he had always wished for.

However, the expectation from a euthanasia venture is far from being a linear, fixed and reproducible rationale. In a specific context, a violent death, a suicide, a suicidal surrender would become the best salvation and an unprecedented final shield. Reason will prefer them because, although they are far from being good, they will at least ensure the gentleness of death.

The accounts of the Greek historian Polybius (202–120 B.C.) report that after the bitter military defeat of the king of Sparta Cleomenes, the latter expressed a final de-sire: to commit suicide in order to have a beautiful and dishonest death (euthanatesai), thus avoiding captivity to his enemies.[2]

In the turmoil of his political disgrace, and his supposed escape, Cicero (106–43 BC) also wished for a good death (euthanasia). Disavowed by his best friend Atticus, he wrote that his death would be a symbol of betrayal and desertion.[3]

Finally, Flavius Joseph tells the story of four lepers who decided to surrender to the guru enemy, preferring to have their throats cut and thus benefit from a "gentler" death, rather than face a death of an uncertain nature outside the city.[4]

Thus, according to Bacon, euthanasia clearly appears to be carried by two exclusive and in some respects quite opposite meanings: on the one hand, that of a gentle death, and on the other, that of suicide, considered to be irreversible and preferable to the torments of a hellish death.

[1] 63 B.C.–14 A.D., Life of the Twelve Caesars, "Augustus", 99.

[2] Polybius [202–120 BC], Histories, V, 38, 9.

[3] Letters to Atticus, XVI, 7, 3.

[4] Jewish Antiquities, IX, 4, 5.

2.1.2. Alleviating Care, the Contemporary Medical Response to the Wish for Gentle Death

As early as under the First Dynasty in Egypt, at the end of the fourth millennium B.C., end-of-life houses were founded in temples. The future doctors learned the art of treating the dying. Then religions, including Christianity, took care of the weak and the dying.

Thus, in the Middle Ages, the brotherhoods of the "good death" and the Hotels Dieu provided emotional, spiritual, social support and care to the needy and the incurable.

Much later, on the initiative of the Association of the "Dames du Calvaire", founded in 1842, Francis Bacon, an English politician, scientist and philosopher, urged medicine — through two texts published in 1605 and 1623 and rather similar in content — to commit itself to two pre-rogatives: to provide care and to alleviate pain until the last breath.

The initial dark and disturbing meaning of euthanasia then became fleeting, giving way to that of a gentle death accompanied by care and comfort. This was Bacon's new paradigm, which was summed up as euthanasia exterior (physical euthanasia). Indeed, according to him, "it is the task of the physician not only to restore health, but also to alleviate suffering and pain, not only when a softening is conducive to healing, but also when it can help one to pass away peacefully and easily, in the manner of Augustus, Anthony the Pious and Epicurus, whose deaths were much like a benign and pleasant sleep." In his text, Bacon (1991) was the first — if not, one of the first — to formulate a plea in favor of euthanasia. In his 1623 publication, F. Bacon (1991) reasserted the thought brought out in his article published in 1605. He insisted on the role of the physician, who should no longer limit himself to curative action, but should also work to alleviate the pain of illnesses, even when these were to prove fatal.

The aim was to ensure a gentle and peaceful death, and to "help those who are dying to leave this world more gently and easily. With this new paradigm dedicated to the end of life, Bacon thus made explicit his notion of external euthanasia which prepares the body — which, according to him, is very highly desirable — and which is in no way comparable to the notion of internal euthanasia, which aims at preparing the soul" (Bacon, 1623).

Bacon's approach seems pragmatic, rational and leaves no room for misunderstanding by the practical momentum it suggests. According to him, the euthanasia of the body is precisely about a total attenuation of pain, if possible, and is not a cryptic method that induces premature death. It would thus be an outlet facilitated by the absence of pain.

2.2. Utilitarianist Euthanasia

Utilitarianism, a doctrine in political philosophy or social ethics, recommends working, or not, to maximize collective well-being, understood as the sum or the average of the well-being of all sentient and affected beings.

This doctrine thus conceives the waste of well-being as an injustice. Theorized by J.S. Mill (1863) on the foundations established by Jeremy Bentham (1748–1832), "utilitarianism designates the doctrine" which recognizes utility as a rule, without wishing to designate this or that way of applying this rule. "It is also the principle according to which the only thing desirable as an end is happiness, the presence of pleasure and the absence of pain, otherwise formulated" (Mill, 1863). The usefulness of life would thus depend on the preponderance of pleasure over pain, its defect would de facto formulate the uselessness of the latter. Given these considerations, consequentialist theories are in fact the most important and robust set of arguments for the proponents of euthanasia.

In this regard, the Scottish philosopher D. Hume was quick to point out that, however well structured, the Thomistic thesis,[5] pamphlet against euthanasia, had little resistance to consequentialist theories. It should also be noted that the theories that make dignity or existential rights the centerpiece of bioethical reflection may, in view of the interpretation they give to these notions, authorize — if not at least recommend — the practice of euthanasia.

Moreover, the utilitarianist concept, the spearhead of contemporary "pro-euthanasia" associations, is very old. According to Plutarch, a Greek-born philosopher, biographer, moralist and leading thinker of ancient Rome (46–125 AD), the fate of a newborn child did not depend on the will of its father. The latter had to submit it to the attentive

[5] Thomas Aquinas, Summa Theologica, II-II ae, Q. 64, art. 5.

examination of the oldest. If the newborn child was strong and free of defects, the wise men would order his father to raise him and grant him one of 9,000 plots of land. On the other hand, if the child's condition was marked by any weak-ness or deformity, the death sentence for him was without appeal, considering that this was preferable on the one hand for the child himself and on the other hand for the rest of the community.[6] For his part, Strabo (58 BC–25 AD) reports the practice to Ceos of a form of population regulation justified by a concern for food security. All people reaching the age of sixty were forced to drink hemlock (a true elixir of death!) (Strabon, 1971). According to Valerius Maximus (1st century BC–1st century AD), a lethal preparation based on hemlock, was "offered" to any person likely to provide before the Six Hundred (Sen-ate of the city) details and reasons for his will to kill himself. "A courageous procedure tempered with kindness, not allowing one to leave life without reason, while offering to the one who clearly knows why he wishes to leave it a quick way of fulfilling his destiny" (Valere, 1995).

This concept of utilitarian death is also widely reported by Thomas More (1478–1535) in his book Utopia. Whenever the illness was deemed incurable and burdened by continuous and unbearable suffering, magistrates and priests would commit the sick person, who had unfortunately become a burden both to himself and to the community, to accept death. He would have the choice of carrying out this task himself or to invest a third party in it. His wise and saving action would be a deliverance and a mark of piety towards the deities. In order to do this, the patient would abstain from eating or would choose to be put to sleep. It is important to emphasize, however, that no suspension of care or killing was involved against will. Those who took their own lives without the approval of the priests and the Senate were deprived of a burial (More, Prévost, 1978). Far from being the defender — because very opposed — of the right to suicide, Thomas More reports only in his work a description of the dynamic and rational system of thought of the Utopians (More, Prévost, 1978).

This concept was also widely observed among the Eskimos of Nunaga, the Chukchee of Northeastern Siberia and the Yuit of the St.

[6] "Vie de Lycurgue", Vies parallèles, Paris, Les Belles Lettres, t. I, at 143.

Lawrence Islands. In these communities, euthanasia represented the ultimate and obligatory stage of an honorable life. The elderly person, unfortunately becoming much less necessary to family life and incapable of deploying sufficient strength to run after the dogs, would charge his favorite son to help him die by either stabbing, shooting, harpooning, strangling or hanging him. As in the case of the E people of Northeastern Siberia, the "old" person who was bedridden or simply exhausted by life had to make a vow to be killed. Often causing fear and amazement, this request was in practice a moral constraint for the community and forced it to respond. If the request was maintained and strongly reaffirmed, it became irreversible. Indeed, it could provoke the Kelets (evil spirits) who could not find appeasement as long as the "deadly" enterprise was not completed. Once the decision had been taken and the "executioner" known, the work was very quickly accomplished (Baechler, 1981).

2.3. Euginistic Euthanasia: Hygienists, Eugenists and State Crime

Among the most outstanding research interests of Sir Francis Galton (1822–1911), anthropologist, explorer, geographer, inventor, meteorologist, writer, proto-geneticist, psychomotor therapist, British statistician and cousin of Charles Darwin, was the establishment of a process that would allow the systematic and scientific selection of what could be considered the elite of humanity — or rather of the United Kingdom. As such, together with his disciple Karl Pearson, with whom he founded "Biometrika", a journal devoted to this concept, he is undoubtedly considered the founder of the British school of biometry and eugenics. The admitted objective of this selection process was to cleanse the hereditary heritage of all degenerative factors. In 1888, Georges Vacher de Lapouge, a French anthropologist, magistrate, then librarian, took up the challenge again by developing the racist theory outlined by Gobineau at the end of the 19th century and theorizing eugenics. Through his work, Vacher de Lapouge established that eugenism was the result of eugenics. In the wake of this, anthropologists, doctors and biologists, supported by a strong popular support, created societies and journals oriented towards eugenics. From 1907 to 1940,

the appropriation of this principle and its accommodation worked at the highest level in many states. In fact, in 35 states in the USA, two Canadian provinces, Germany, Denmark, Finland, Norway, Sweden and Switzerland were promulgated laws of sterilization, voluntary or imposed, against people suffering from pathologies deliberately supposed to be hereditary, strongly considered as dangerous for society. Among these illnesses were mental disorders of all degrees of severity, sexual offences and so-called socially dangerous tendencies, which, according to several experts at the time, were more a form of social deviance and in no way a pathological state, even when admitting an anachronistic interpretation (Morange, 1996) (Veuille, 1999). Charles Richet, while awarded the Nobel Prize for Medicine and Physiology in 1913, wrote in 1912, the year of the creation of the French Eugenics Society, in "La Sélection Naturelle", that he "saw no social necessity in preserving (the) abnormal children." Alfred Hoche, a psychiatrist, and Karl Binding, a lawyer, had "Die Freigabe der Vernichtung lebensunwerten Lebens" [The Liberalization of the Destruction of a Life Not worth Living] published in Leipzig in 1920. Although the title is self-explanatory, the various — often contradictory — critical analyses dedicated to this publication hardly revealed the inhibiting character of forced eugenic euthanasia.

These analyses are strongly corroborated by the writings of Karl Binding: "The will to live of each individual, even of the sickest and most tortured human beings, must be respected (...). It goes without saying that there will be no question of liberalizing the homicide of a mentally handicapped person as long as he is happy with his life" (Morange, 1996) (Veuille, 1999). The investigation of a request for euthanasia was carried out by a commission, whose deliberations only took place — upon request — if it was unanimous. The introduction of a request for liberalization (request for euthanasia) was thus made either by the patient himself, who was suffering from a fatal illness, or by the patient's doctor or by a relative delegated to do so. If it was established that the request was admissible, an expert was appointed to carry out the act and a report would ultimately be drawn up for the commission.

Contrary to the doctrine of K. Binding, which incited to respect the desire to live of the sick including those supposedly useless to the society, that of A. Hoche advocated the concept of "mentally dead"

individuals whose lives would be a burden on the community. This life was judged to be worthless, precisely in the context of the time, marked by a competition between nations, which made them to free them-selves from any elements that would disable their ascent and excellence (Goffi, 2004).

In 1925, Hitler completed Mein Kampf, a work in which he exposed, in a style loaded with hatred, his conception of a hegemonic, bellicose, racist world and compiled, while supporting them, all the eugenic theses. In 1933, largely in view of the dominant socio-political context, public opinion was ready to adopt these theses. As a matter of fact, at the congress of April 1933, having gathered in Bremen nearly 500 eugenists, it was declared: "All unproductive life is considered a life without value." Under the express impulse of Hitler a committee of euthanasia was then created. Composed of 25 doctors, including 7 holders of the chair of neurology and psychiatry, it stood under the absolute authority of Professor Linden.

All the structural tools were thus ready to carry out the operation launched by Hitler against the mentally ill on September 1, 1939, bearing the name Aktion T4, and also Aktion Gnadentot (Grace of Death). It should be noted that this "makabre" action was directed from number 4 Tiergartenstrasse in Berlin. Recruitment of patients eligible for Aktion T4 was determined by their ability to take on a job. All hospital and asylums directors were asked to fill out a questionnaire to determine the capacity of each res-ident to work. Patients who were declared unfit for work, sometimes simply because of the protecting spirit of the managers of these institutions, were transferred to "charitable" foundations, not for hospital care as had been announced, but for certain death. The reasons for death most often mentioned were then bronchopneumonia or idiopathic weight loss. The organization of this dark enterprise began with the transfer of patients to the said charitable foundations, which was carried out by a company created specifically for this purpose. In order to keep away the curious on-lookers, large signs surrounding these foundations warned of a risk of contagion. The nursing staff, recruited on a voluntary basis, had to pledge allegiance to the Reich, committing themselves to absolute obedience and infinite discretion. Any violation of this pact would result

in the certain death of the offender. However, in the face of exacerbated and overt opposition from religious authorities who were silent and docile at first, and a significant fringe of the army and a growing number of doctors, Hitler suspended the macabre work on August 24, 1941. The death toll attributed to Aktion T4 amounted to 100,000 disabled and 75,000 elderly (Bayle, 1950) (Ternon and Helman, 2000).

The disclosure of these crimes in the post-war period had the effect of discrediting any type of so-called humanitarian euthanasia. In his book "L'Art de mourir: Défense et technique du suicide secondé", Charles Binet-Sanglé, in 1919, reiterated the reasoning behind the right to assisted suicide and described several modalities of painless suicide. In the same work, he insisted on the interest of setting up a state-funded euthanasia institute. However, regardless of the formulation of super-vised suicide, clandestine, assisted or not, all these practices refer to hygienic and eugenic crimes practiced in the name of the State. Moreover, a few decades later, a few trials marked public opinion, to say the least (Daviani, 1970; Putte, 1962). Nevertheless, it should be said that the acquittal of the perpetrators of these homicides was the norm, notwithstanding the fact that they did not correspond to any euthanasia notion. Nevertheless, they have the merit of having participated to some extent in advancing the cause of euthanasia.

2.4. Compassionate Euthanasia

One of the most striking episodes and undoubtedly one of those that best illustrate the compassionate nature of euthanasia is the epilogue of the six Russians taken charge of by Pasteur at the Hôtel-Dieu. According to Léon Daudet, then a young medical student, they were six Russians from a rural area, bitten by a wolf most probably suffering from rabies and transferred to Paris to be cared for by Pasteur's team at the Hôtel-Dieu. Using the usual protocol dedicated to this type of pathological situation, Pasteur had them injected with anti-rabies serum for eight days. Unfortunately, on the ninth day, the patients showed a noticeable worsening of their condition and complained of unbearable systemic pain, to the point of imploring the health care team to give them a certain and immediate death. "After consultation between the hospital's chief

pharmacist (...) and Pasteur, the decision was made. The pharmacist prepared five pills — one of the six patients having died, which were administered to the other five with all the discretion that is customary in such cases. When silence fell, (...) we all began to cry in horror. We were a nervous wreck, devastated" (Daude, 1915). The decision was taken in this way, collegial and secrete.

Although singular, the experience is part of the type of decisions that the con-science of all caregivers is confronted with and is de facto understood as a common fact of medical practice. However, is it acceptable and conceivable to admit a continuum between a specific case and the law, and if so, to consider that the reasons are always specific and not stereotyped, recognized only by certain individuals refractory to any civil law. It will thus be difficult to claim to be able to decide on the primacy of compassion and make it a right. "A fierce struggle to make compassionate euthanasia a right." Clearly, the twentieth century is marked by declarations in favor of compassionate euthanasia.

Following the creation of the Voluntary Euthanasia Association (VES) in 1935 in England, renamed EXIT, and the Society for the Right to Die in the United States in 1983, renamed the Euthanasia Society of America in 1975, many associations were created in the late 1970s. They all had as a common claim the right to die with dignity. They formed a world federation for the right to die. The number of their members is estimated at 500,000 worldwide. On July 1, 1974, Le Figaro, a newspaper whose editorial line has always been resolutely right-wing, published a manifesto in the form of a plea for the right to euthanasia. The latter was signed by 40 eminent academics and doctors, including three Nobel Prize winners: "We, the undersigned, declare, for ethical reasons, to be in favor of euthanasia. We believe that there is a mature moral conscience in our societies to develop a rule of humanitarian conduct regarding death and the dying. We deplore the insensitive morality and legal restrictions that impede the ethical case for euthanasia." In this text, the signatories of this manifesto implicitly demanded the awakening of the collective conscience and urged public opinion to overcome certain unfounded traditional concepts that would lead to suffering and agony at the time of death. Alas, this manifesto will not arouse much interest and has still to happen. On November 17, 1979, the militant article by

Michel Lee Landa, a Franco-American writer with the title “Un Droit” (A Right), published worldwide, would be the genesis of the Association for the Right to Die with Dignity in 1980. The article, which advocated the need to recognize the right to die voluntarily and to be helped to do so, provoked strong reactions of support — for the legalization of this right — for people of very advanced age, for patients suffering from serious pathologies and for those suffering from serious handicaps. Three years after its creation, the ADMD has several thousand members. Its objective was to be a watchdog on the laws and regulations governing the right of individuals to be able to choose the conditions of their end of life. It also functioned as a movement of opinion, creating a kind of driving force to advance the debate of ideas in its favor (Pohier, 1998). The three main objectives of ADMD are: “The right to control pain, the right to refuse therapeutic persecution and the right to voluntary euthanasia, each member being free to claim for themselves only one or the other of these rights, but recognizing that the association must fight to ensure that all three rights are recognized and achievable for all those who would claim them” (Pohier, 1998).

In 1980 near Munich, Dr. Hacketal opened the Eubois Clinic for patients who ex-pressed a need for assisted suicide. Dr. Peter Admiraal took over this approach and set up a unit with a similar objective at the St. Hippolyte Hospital in Delft (ND). In 1990, in Detroit, Michigan, Dr. Jack Kevorkian’s initiative was singular to say the least. Kevorkian developed a suicide machine that he named the Mercytron. Its use was based on the combination of three infusion solutions, one of serum to dilate the venous capital, the second of Pentothal to sedate the patient, and the third of potassium to ultimately cause cardio-circulatory arrest. It should be noted that Dr. Jack Kevorkian will be charged with four counts of assisted suicide, which will be ac-companied by four acquittals. However, on April 13, 1999, Dr. Jack Kevorkian will be sentenced to between ten and twenty-five years in prison for the second-degree murder of Thomas Youk. As Dr. Jack Kevorkian stated in one of his statements that he never understood a word his patient said, the assistance in suicide qualification was never retained.

III. Deadlock in the Specification of the Euthanasic Act

Generally speaking, the care for patients at the end of life, whether hospitalized or at home, who are most often overwhelmed by significant suffering, is based on well-codified procedures. The latter respond to the logic of syndromic treatment whose enumeration, in view of the risks it evokes, allows the following classification: high-dose analgesia therapy; active reduction or cessation of intensive care, suspension of all extracorporeal vital substitutes, active or passive assistance in suicide, and finally inoculation of lethal substances. Their misuse is often envisaged for euthanasic purposes, either at the request of the patient himself or herself, or on a patient who is unconscious or unable to exercise their will, or, finally, against the patient's will. However, the five above-mentioned acts constituting the conduct to be followed in caring for the patient at the end of life — palliative care — require, on the one hand, clarification as to the absence of treatment. Indeed, this situation can only be considered as an act on the condition that it derives from a medical decision and not from negligence. On the other hand, a clarification concerning the often-concomitant practice of the various acts mentioned above. The possible association of several acts would heighten the action of this or that molecule which would ultimately anticipate the fatal event. There would thus be no difference between a strongly analgesic cocktail, or even sedation, and a frankly lethal cocktail, neither in terms of technique of application nor in terms of consciousness.

In this context of lack of consensus around the euthanasic act, two totally opposed visions remain. One is held by those who advocate the generalization of palliative care, such as JALMALV, SFAP, together with all the religious authorities, insisting on the total opposition between the first three acts, a veritable range of supportive and accompanying care, on the one hand, and acts 4 and 5 on the other hand, which constitute an assisted suicide and an assassination, or even a premeditated murder, respectively. The other, very amply supported by the signatories of the "appeal of the 132", a tribune published by the ADMD in France Soir, Libre-Pensée, Les Libres Exaministes Belges, supports the principle of a continuum between the five acts. The consequences of each of

these acts would be closely involved in the ex-tension of their effects. Thus, according to this thesis, the cessation of respiratory substitution unfortunately induces death and would de facto imply the complicity of the caregiver, if not at least his or her complacency.

IV. Conclusion

At the end of this reflection a question remains open: that of the definition of euthanasia. Should it be an adaptive concept and therefore vary according to the various situations? Or should it avoid diversity?

It is common that the works that have been devoted to it rank it either according to an active modality — and in this case the act of deliberately killing a patient with or against his or her will is motivated by reasons that are, after all, clear in relation to his or her pathology, physical or moral suffering. Also included in this modality are actions useful for assisted suicide. Either in passive modality — which would mainly rely on suspending all organic sup-planting, limiting active therapeutics and the use of analgesics whose escalation of doses is strongly responsible for the advent of death. Attempting in this way to circumscribe the euthanasic act would first of all oblige us to grasp the versatility of the intention that carries it. It would therefore be erroneous to believe that this would amount to simply documenting the fields of possibilities in which the euthanasia question would arise. Beyond a banal, well-standardized definition, it is a concept that, by dint of use, imposes itself on humanity in the face of the test of time. In light of the expectations of a large part of contemporary societies, the question of euthanasia should be approached with serenity, but also head-on, as it is always raised and imposed. Thus, it is in no way useful, but rather harmful, to avoid the questioning inherited from the legitimacy of compassionate homicide under certain conditions, from the prohibition of murder when the pain is unbearable and rebellious to any painkiller, and from the need to free one-self from religious dogma where euthanasia is an imposed death that would be op-posed to natural death. This dogma sounds like the common assumption according to which, however violent it may be, natural death belongs to the one who under-goes it, whereas an imposed death, even if it is

an absolute choice, would be foreign to him. Nevertheless, the ridge line that differentiates a natural death from an imposed death is often sinuous and very imprecise, for so-called natural death is never devoid of violence. Thus, rather than the relentless and lasting violence imposed by natural death — in some patients at the end of life — the moral violence of a life-saving euthanasia is unequivocally preferable.

References

1. Abiven, M., (1990). *Pour une mort plus humaine: expérience d'une unité hospitalière de soins palliatifs*. Paris, InterÉditions.

2. Abiven, M., Chardot, C., Fresco, R. and Glorion, B., (2000). *Euthanasie. Alternative et controverse*. Paris: Presses de la Renaissance.

3. Aurenche, S., (1999). *Leùthanasie, la fin duǹ tabou?* Paris: ESF editeur.

4. Bacon, F., (1991). *Du progrès et de la promotion des savoirs (1605)*. Paris: Gallimard.

5. Baechler, J., (1981). *Les suicides*. Paris.

6. Bayle, F., (1950). *Croix gammée contre caducée*. [S.l.]: F. Bayle.

7. Bayle, F., (1950). Croix gammée contre Caducée. Les expériences humaines en Allemagne pendant la deuxième guerre mondiale. *Imprimerie nationale, Neustadt-Palatinat*, 1, p. 521.

8. Binding, K. and Hoche, A., (2006). *Die Freigabe der Vernichtung lebensunwerten Lebens*. Berlin: BWV Berliner Wissenschafts-Verlag.

9. Daudet, L., (1915). *Souvenirs des milieux politiques, littéraires, artistiques et médicaux*. Paris: Nouvelle Libr. Nationale.

10. Goffi, J., (2004). *Penser l'euthanasie*. Paris: Presses Universitaires de France.

11. Goffi, J., (2008). Le dilemme sans fin de l'euthanasie. *Le Monde*, [online]. Available at: https://www.lemonde.fr/societe/article/2008/04/05/le-dilemme-sans-fin-de-l-euthanasie_1031346_3224.html#:~:text=Jean%2DYves%20Goffi%2C%20professeur%20de,le%20devant%20de%20la%20sc%C3%A8ne [Accessed 22.12.2020].

12. Hocquard, A., (1996). *L'Euthanasie volontaire*. Paris: PUF.

13. Maret, M., (2000). *L'euthanasie. Alternative sociale et enjeux pour l'éthique chrétienne*. [Saint-Maurice] Suisse: Saint-Augustin.

14. Mill, J., (n.d.). *Jurisprudence*, pp. 48–49.

15. Morange, M., (1996). *Eugénisme*. in Canto-Sperber.

16. More, T., Prévost, A., Schumann, M. and More, T., (1978). *L'Utopie*. Paris: Mame, p. 549.

17. Pohier, J., (1998). *La mort opportune. Les droits des vivants sur la fin de leur vie*. Paris: Seuil.

18. Rachels, J., (1975). Active and Passive Euthanasia. *New England Journal of Medicine*, 292(2), pp. 78–80.

19. Strabon, (1971). *Géographie. VII, 10, 5, 6*. Paris: Les Belles lettres.

20. Ternon, Y. and Helman, S., (2000). *Le massacre des aliénés*. Castermann: Abiven, pp. 36–44.

21. Valere, M., (1995). *Fait et dits mémorables, II, VI, 7d*. Paris: Les Belles Lettres, pp. 181–182.

22. Veuille, M., (1999). Eugénisme. In: D. Lecourt, ed., *Dictionnaire de la pensée médicale*. Paris: PUF.

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Genome-Editing Technologies in Biomedical Research: The Regulatory Conditions for the Development

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Abstract: Significant progress has been made in the development of genetic technologies in recent decades. Currently, high-performance sequencing and, most importantly, genome editing technologies are widely used and available for laboratories in Russia. Existing technologies are not without drawbacks that significantly hinder further development, in addition, all the necessary reagents and materials, as well as equipment, are produced exclusively abroad. The review highlights the international experience of using genome editing technologies for the treatment and prevention of genetic diseases, vector-borne and viral infections, it offers recommendations for the development of this area in the Russian Federation. Attention is drawn to the legal and ethical regulation, mainly at the level of basic principles. The conclusion is formulated on the need for accelerated adaptation of basic ethical and legal principles for genome editing activities in scientific biomedical activities.

Keywords: genetic technologies, genome editing, CRISPR/Cas, biomedical sciences, regulation, ethics, law

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Contents

I. Introduction

The last decades of intensive development of genetic technologies have been marked by a number of impressive achievements, including the decoding of the complete human genome, the development of the single cell DNA sequencing technology, and, finally, the development of genome editing technologies. Highly efficient genome editing technologies are based on the ability to implement precisely directed double-stranded DNA breaks in the chromosomal region of interest. Numerous non-specific breaks in the DNA occur during the natural process of meiosis, or can be artificially caused by ionizing radiation (Brinkman et al., 2018; Vitelli et al., 2017). Further repair processes can occur by one of two main mechanisms: non-homologous DNA end joining (NHEJ) or homologous recombination (HR). During NHEJ, DNA ends are ligated with minimal enzymatic processing at the end-junction site, while in HR, an intact sister chromatid is usually used as a repair template (Rulten and Grundy, 2017; Wang, Lee and Zha, 2020).

Studies with highly specific genome targeting demonstrated stimulation of both NHEJ and HR in yeast and mammalian cells and, thus a way to programmed genome editing was obtained. Sometimes, errors occur during NHEJ repair, resulting in small local insertions and deletions. These mutations can cause inactivation of the edited gene (Zischewski, Fischer and Bortesi, 2017).

Currently, three powerful classes of nucleases that can be programmed to produce double breaks in essentially any desired target are used in molecular biology: zinc finger nucleases, transcriptional

activator-like effector nucleases (TAL nucleases), and CRISPR-Cas nucleases. At present, it is CRISPR-Cas that dominates research laboratories around the world, since other methods are less effective, more costly, and laborious (Anzalone, Koblan and Liu, 2020; Germini et al., 2018).

Scientists Emmanuel Charpentier and Jennifer Doudna were awarded the Nobel Prize in Chemistry for 2020 for the development of a genome editing method based on the CRISPR/Cas9 system (The Nobel Prize in Chemistry 2020, 2021).

II. Limitations of Modern Genome Editing Techniques

The target of using genome-editing nucleases, in fact, is only producing double-stranded breaks of chromosomal DNA. The main criterion of efficiency is the specificity of the genome-editing platform for a clearly defined region of the genome and the absence of breaks in other loci. However, everything that happens after the rupture is determined by the mechanism of the cellular DNA repair, two variants of which were described earlier. Most somatic cells in higher eukaryotes start the NHEJ process with the concomitant occurrence of insertions and deletions more often than copy sequences from the donor DNA provided. This is acceptable if the purpose of editing is to knock out a gene or a complex of genes, but it significantly limits the possibility of introducing required nucleotide sequences. In studies (Karagyaur, Rubtsov, Vasiliev and Tkachuk, 2018; Paix et al., 2017), limited success has been achieved in modulating the ratio between the target and the mutant product, but so far no universal solution has been found, and for some types of cells, NHEJ remains the most frequently occurring repair method. Several recent publications report that small molecule inhibitors of key enzymes in the NHEJ process can be effective, but more research is needed to create more reliable reagents (Bischoff, Wimberger, Maresca and Brakebusch, 2020; Li et al., 2017). Another way of increasing the efficiency of insertion of the target gene is the modification of the donor DNA molecule, linking the donor sequence with the guide RNA, and using natural mechanisms for inserting the

desired fragments (Chen and Knoepfler, 2016; Chuai et al., 2018; Dyikanov et al., 2019; Long et al., 2018).

On the other hand, all DNA editing platforms have high but limited specificity. One of the latest studies has shown the possibility of increasing the specificity of CRISPR-Cas by modulating the Cas9 protein and guiding RNA. It depends on the application how important is the absolute specificity of the editing system, as well as the absence of mutagenic potential. In many model organisms, there are ways to prevent the expression of a mutant gene, for example, by knocking it out and replacing it with a wild-type genome. We can rely on these mechanisms when editing the genome of plant or bacterial cells, as well as when creating humanized animal models for pharmacological research (Hackett et al., 2018; Hua, Wang, Huang and Wang, 2017). Even in some medical applications, off-target mutations may be acceptable if they do not lead to a disease, but this aspect is the most ethically vulnerable (Brokowski and Adli, 2019).

According to the established bioethical literature, international and national ethical (bioethical) principles, the doctor and the researcher should always be guided by the principle of non-harm, and the degree of the existing risk should not exceed the existing problem (real, not imaginary). According to the Code of Professional Ethics of a Doctor of the Russian Federation (adopted by the National Congress of Doctors on October 5, 2012), a doctor engaged in scientific activities should not use his scientific knowledge to the detriment of the health and safety of the patient or society. The priority of the patient's interests is established as a principle and in Art. 4 of the Federal Law No 323-FZ dated 21.11.2011 "On the fundamentals of the public health protection in the Russian Federation".

III. Development of New Genome Editing Platforms

Genome editing will probably remain a widely used tool in both scientific research and commercial and medical fields. However, there arises a question: is CRISPR-Cas the last word in programmable nucleases, or perhaps there is something even better on the horizon. At the moment, it is difficult to imagine a system that is significantly

simpler than recognition of a gene by a complementary matrix and cleavage by a single protein. It is possible to develop a chemical system based on low molecular weight synthetic compounds that combine DNA recognition with its cleavage. Research aimed at achieving this goal has been going on for decades — from triplex-forming oligonucleotides to peptide nucleic acids and polyimines (Eid, Alshareef and Mahfouz, 2018; Koonin, Makarova and Zhang, 2017; Lee et al., 2018), but the development of the platform with adequate specificity and efficiency is still far away. It seems that new methods of genome editing will be discovered through research into natural processes rather than through optimization of CRISPR techniques. A variant of gaps-induced genome editing is CRISPR-mediated base editing. This technology uses nickase Cas9, which edits only one strand of the target DNA. Conversion of cytisine to uracil within a few base pairs closest to the RNA binding site results in changes of expression in this very narrow region. Future uses of this approach may include modification of individual alleles of human genes.

IV. Application of Genome Editing Technologies in Medicine

At the moment, a large number of attempts to use genome editing technologies in clinical practice have been described. FDA has approved a large number of clinical studies involving somatic cell genome editing for phase I clinical trials. The earliest studies used zinc finger nucleases to knock out the CCR5 receptor gene in T lymphocytes of HIV-positive patients (Liu et al., 2017), this modification makes T cells resistant to the virus. In the future, it is planned to edit the genome of lymphocyte progenitor cells and even individual cells of the human embryo (Cyranoski, 2019).

TAL nucleases have been used to enhance the efficacy of CAR-T cell therapy (Lucibello, Menegatti and Menger, 2020); in addition, two studies using CRISPR/Cas9 have been approved for this purpose. These examples are based on genome editing of cells previously isolated from the body, followed by administration to the same patient from whom the collection was made (autologous biomedical cell products).

Such *ex vivo* procedures allow for easy delivery of editing systems into cells, as well as the ability and preliminary characterization of edited cells. During the development of cell therapy methods, genome editing will become an integral complement to them. In many cases, cell therapy is not possible (for example, it is impossible to isolate all or even most of the target cells). Currently, clinical trials of agents for the treatment of hemophilia and lysosomal storage diseases are underway, based on the delivery of zinc finger nucleases in vivo by viral vectors. Thus, the genome of hepatocytes, which are classified as the type of cells that are readily available for introduction, is edited. Delivery into other organs *in vivo* will require the creation of new vector and non-vector approaches and, possibly, the creation of specific lines of genetically modified stem cells. Active research is directed towards the treatment of other genetic diseases, including sickle cell anemia and muscular dystrophy. As with any medical application, genomic editing systems must be proved to be effective and safe (Gerace et al., 2017; Kick, Kirchner and Schneider, 2017; You et al., 2019).

V. Human Embryo Genome Editing

Due to the ease of editing the genome using the CRISPR platform and, accordingly, the wide potential for abuse of the technology, there is a considerable interest in the prospects for editing the genome of the human embryo. The main method of application is the delivery of editing agents into the cells of an embryo created by in vitro fertilization. In the future, it may be more appropriate and ethically acceptable to edit gametogenic progenitor cells in the future parents. The advantage of embryonic correction of gene alleles corresponding to pathological conditions is that they will disappear from the genome forever. However, there is a risk that trying to correct the genetic code of an unborn child could do more harm than good. Modern genome editing technology does not have sufficient efficiency and specificity to fully guarantee safety. Mutations arising at off-target chromosome loci as a result of the introduction of editing constructs can affect the child's body and be transmitted from generation to generation, and their effects will not always be benign, predictable or reversible.

The world's first operation to edit the genome of a human embryo was performed in 2018 in China. Chinese geneticist He Jiankui performed *in vitro* fertilization and then edited the genomes of the resulting embryos using CRISPR/Cas9 technology, creating an artificial mutation in the CCR5-Δ32 gene, which should provide future children with immunity to the human immunodeficiency virus. As a result, the first twin girls in the history of mankind were born with an edited genome ("The CRISPR-baby") (Greely, 2019).

Ongoing research will make embryonic genome editing safer and more efficient, and it seems inevitable that it will eventually be widely used. At the same time, it is important to discuss both legal (Mokhov, Levushkin and Yavorsky, 2020) and ethical (Cribbs and Perera, 2017) issues related to the editing of the human embryo genome.

VI. The Conditions for the Development

During the development of molecular biology and biomedicine, genome editing technologies are being improved and developed, their safety and effectiveness are increasing. The main leaders in this area of research are China, the United States and the EU. Russian scientists are also actively involved in global genetic research. According to the level of qualification, Russian researchers are comparable to employees of the world's leading genetic laboratories, which allows not only to effectively use, but also to develop modern genome editing technologies (Rebrikov, 2021). However, to date there is a significant lag in the country's production of its own equipment, reagents, materials, software and digital databases necessary for the introduction of the developed genetic technologies in industrial production and medical practice in Russia.

In the modern world, the ability to have their own genetic technologies and molecular platforms for genome editing is certainly necessary both for the development of bioeconomics and for ensuring the biosafety of the state. Recently, the Russian Federation has taken a number of strategically important steps to accelerate the development of genetic technologies to achieve the goals of the national bioeconomy and biosafety of the country's population. The legal basis for the accelerated

development of this scientific and technical direction in the country was a number of policy documents: the Decree of the President of the Russian Federation dated 28.11.2018 No 680 "About the development of genetic technologies in the Russian Federation", the Resolution of the Government of the Russian Federation dated 22.04.2019 No 479 "On the approval of the Federal scientific and technical program of development of genetic technology in the years 2019–2027", and the Order of the Government of the Russian Federation dated 26.10.2019 No 2535-R "On the approval of the list of organizations on the basis of which world class genomic research centers are established".

An important practical step towards the implementation of these documents was the signing in 2020 of an Agreement on Cooperation between the Government of the Russian Federation and Public Joint Stock Company "Rosneft Oil Company"[1] in order to solve the problems of accelerated development of genetic technologies in the Russian Federation and the country's entry into the world's leading positions in this field of science and technology.

One of the important conditions for solving these strategic state tasks is the creation of a comfortable regulatory environment for the development of national genetic technologies, in the form of improving the regulatory framework and eliminating administrative and technical barriers. A special working group of experts has been established under the Presidium of the Council for the Implementation of the Federal Scientific and Technical Program for the Development of Genetic Technologies for 2019–2027 to coordinate the development of legal regulation in the field of genetic technologies, including genomic editing. Under the auspices of the working group, within the framework of the state task of the Ministry of Science and Higher Education of the Russian Federation, expert and analytical studies on the topic "Legal regulation of accelerated development of genetic technologies: scientific and methodological support" are being conducted at the Kutafin Moscow State Law University.

[1] Order of the Government of the Russian Federation dated 02.03.2020 No 481-r.

Another prerequisite is the launch of an import substitution program aimed at reducing the dependence of the development of national genetic technologies on foreign equipment, reagents, materials, software and digital databases.

Against the background of solving a number of scientific and technical tasks, first of all it is necessary to ensure the priority of the humanistic approach at the stage of solving questions about the possibility of practical application of genome editing technologies in medicine, since the introduction of any new medical technology potentially entails risks for the health and life of patients. Existing international law and relevant national legislation clearly classify the preservation of the genome as a fundamental human right.[2]

In terms of the level of knowledge intensity and the speed of development, genetic editing technologies are quite comparable to the most advanced digital technologies, which makes it possible to combine them with the general concept of "High Technologies of the 21st Century". A common characteristic of these high technologies is the situation of a large time gap between the actual beginning of their practical use and the formation of the legislative and regulatory framework governing the process of their official introduction and application. In the context of these realities of the 21st century, it seems reasonable to form and develop a new direction of humanitarian science — the ethics of high technologies. In the system of the Ministry of Health of the Russian Federation, there is an Ethical Council that conducts ethical expertise when deciding on the possibility of conducting clinical trials of new drugs in humans (Khokhlov, Chudova and Tsyzman, 2018). By analogy with this traditional approach for medicine, the idea of creating a specialized collegial expert body to consider the possibility of conducting the first clinical studies of genetic technologies in humans should be considered (Mokhov and Yavorsky, 2020).

[2] The Universal Declaration on the Human Genome and Human Rights (adopted on 11.11.1997 by the General Assembly of the United Nations). Available at: https://www.ohchr.org/EN/ProfessionalInterest/Pages/HumanGenomeAndHumanRights.aspx [Accessed 10.07.2020].

VII. Conclusion

In general, the new state policy of the Russian Federation in the field of development of national genetic technologies is aimed at a significant increase in funding and rapid deployment of promising scientific and technological programs at rapid achievement of practical results, the creation of real technologies for high-precision genome editing, and the production of competitive biotechnological products both in Russia and in the world. A striking example of the successful implementation of the new policy of development of national genetic technologies was the fact of using genome editing technology to create the first Gam-COVID-Vac vaccine registered in the world at the National Research Center of Epidemiology and Microbiology named after Honorary Academician N.F. Gamalei (Logunov et al., 2020).

References

1. Anzalone, A., Koblan, L. and Liu, D., (2020). Genome editing with CRISPR-Cas nucleases, base editors, transposases and prime editors. *Nature Biotechnology*, 38(7), pp. 824–844.

2. Bischoff, N., Wimberger, S., Maresca, M. and Brakebusch, C., (2020). Improving Precise CRISPR Genome Editing by Small Molecules: Is there a Magic Potion? *Cells*, 9(5), p. 1318.

3. Brinkman, E., Chen, T., de Haas, M., Holland, H., Akhtar, W. and van Steensel, B., (2018). Kinetics and Fidelity of the Repair of Cas9-Induced Double-Strand DNA Breaks. *Molecular Cell*, 70(5), pp. 801–813.e6.

4. Brokowski, C. and Adli, M., (2019). CRISPR Ethics: Moral Considerations for Applications of a Powerful Tool. *Journal of Molecular Biology*, 431(1), pp. 88–101.

5. Chen, K. and Knoepfler, P., (2016). To CRISPR and beyond: the evolution of genome editing in stem cells. *Regenerative Medicine*, 11(8), pp. 801–816.

6. Chuai, G., Ma, H., Yan, J., Chen, M., Hong, N., Xue, D., Zhou, C., Zhu, C., Chen, K., Duan, B., Gu, F., Qu, S., Huang, D., Wei, J. and Liu, Q., (2018). DeepCRISPR: optimized CRISPR guide RNA design by deep learning. *Genome Biology*, 19(1).

7. Cribbs, A. and Perera, S., (2017). Science and bioethics of CRISPR-CAS9 gene editing: An analysis towards separating facts and fiction. *Yale Journal of Biology and Medicine*, 90(4), pp. 625–634.

8. Cyranoski, D., (2019). Russian 'CRISPR-baby' scientist has started editing genes in human eggs with goal of altering deaf gene. *Nature*, 574(7779), pp. 465–466.

9. Dyikanov, D., Vasiluev, P., Rysenkova, K., Aleksandrushkina, N., Tyurin-Kuzmin, P., Kulebyakin, K., Rubtsov, Y., Shmakova, A., Evseeva, M., Balatskiy, A., Semina, E., Rostovtseva, A., Makarevich, P. and Karagyaur, M., (2019). Optimization of CRISPR/Cas9 Technology to Knock Out Genes of Interest in Aneuploid Cell Lines. *Tissue Engineering. Part C: Methods*, 25(3), pp. 168–175.

10. Eid, A., Alshareef, S. and Mahfouz, M., (2018). CRISPR base editors: genome editing without double-stranded breaks. *Biochemical Journal*, 475(11), pp. 1955–1964.

11. Gerace, D., Martiniello-Wilks, R., Nassif, N., Lal, S., Steptoe, R. and Simpson, A., (2017). CRISPR-targeted genome editing of mesenchymal stem cell-derived therapies for type 1 diabetes: a path to clinical success? *Stem Cell Research & Therapy*, 8(1).

12. Germini, D., Tsfasman, T., Zakharova, V., Sjakste, N., Lipinski, M. and Vassetzky, Y., (2018). A Comparison of Techniques to Evaluate the Effectiveness of Genome Editing. *Trends in Biotechnology*, 36(2), pp. 147–159.

13. Greely, H., (2019). CRISPR'd babies: human germline genome editing in the 'He Jiankui affair'. *Journal of Law and the Biosciences*, 6(1), pp. 111–183.

14. Hackett, J., Huang, Y., Günesdogan, U., Gretarsson, K., Kobayashi, T. and Surani, M., (2018). Tracing the transitions from pluripotency to germ cell fate with CRISPR screening. *Nature Communications*, 9(1).

15. Hua, Y., Wang, C., Huang, J. and Wang, K., (2017). A simple and efficient method for CRISPR/Cas9-induced mutant screening. *Journal of Genetics and Genomics*, 44(4), pp. 207–213.

16. Karagyaur, M., Rubtsov, Y., Vasiliev, P. and Tkachuk, V., (2018). Practical Recommendations for Improving Efficiency and Accuracy of the CRISPR/Cas9 Genome Editing System. *Biochemistry (Moscow)*, 83(6), pp. 629–642.

17. Khokhlov, A., Chudova, N. and Tsyzman, L., (2018). The results of the analysis of the expert work of the Council on Ethics of the Ministry of Health of the Russian Federation. *Meditsinskaya Etika*, 2, pp. 17–22. (In Russ.).

18. Kick, L., Kirchner, M. and Schneider, S., (2017). CRISPR-Cas9: From a bacterial immune system to genome-edited human cells in clinical trials. *Bioengineered*, 8(3), pp. 280–286.

19. Koonin, E., Makarova, K. and Zhang, F., (2017). Diversity, classification and evolution of CRISPR-Cas systems. *Current Opinion in Microbiology*, 37, pp. 67–78.

20. Lee, J., Jeong, E., Lee, J., Jung, M., Shin, E., Kim, Y., Lee, K., Jung, I., Kim, D., Kim, S. and Kim, J., (2018). Directed evolution of CRISPR-Cas9 to increase its specificity. *Nature Communications*, 9(1).

21. Li, G., Zhang, X., Zhong, C., Mo, J., Quan, R., Yang, J., Liu, D., Li, Z., Yang, H. and Wu, Z., (2017). Small molecules enhance CRISPR/Cas9-mediated homology-directed genome editing in primary cells. *Scientific Reports*, 7(1).

22. Liu, Z., Chen, S., Jin, X., Wang, Q., Yang, K., Li, C., Xiao, Q., Hou, P., Liu, S., Wu, S., Hou, W., Xiong, Y., Kong, C., Zhao, X., Wu, L., Li, C., Sun, G. and Guo, D., (2017). Genome editing of the HIV co-receptors CCR5 and CXCR4 by CRISPR-Cas9 protects CD4+ T cells from HIV-1 infection. *Cell & Bioscience*, 7(1).

23. Logunov, D., Dolzhikova, I., Zubkova, O., Tukhvatulin, A., Shcheblyakov, D., Dzharullaeva, A., Grousova, D., Erokhova, A., Kovyrshina, A., Botikov, A., Izhaeva, F., Popova, O., Ozharovskaya, T., Esmagambetov, I., Favorskaya, I., Zrelkin, D., Voronina, D., Shcherbinin, D., Semikhin, A., Simakova, Y., Tokarskaya, E., Lubenets, N., Egorova, D., Shmarov, M., Nikitenko, N., Morozova, L., Smolyarchuk, E., Kryukov, E., Babira, V., Borisevich, S., Naroditsky, B. and Gintsburg, A., (2020). Safety and immunogenicity of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: two open, non-randomised phase 1/2 studies from Russia. *The Lancet*, 396(10255), pp. 887–897.

24. Long, L., Guo, D., Gao, W., Yang, W., Hou, L., Ma, X., Miao, Y., Botella, J. and Song, C., (2018). Optimization of CRISPR/Cas9 genome editing in cotton by improved sgRNA expression. *Plant Methods*, 14(1).

25. Lucibello, F., Menegatti, S. and Menger, L., (2020). Methods to edit T cells for cancer immunotherapy. *Methods in Enzymology*, 631, pp. 107–135.

26. Mokhov, A., Levushkin, A. and Yavorsky, A., (2020). Genome Editing of Human Embryo: Allow or Prohibit? *Journal of Advanced Research in Law and Economics*, 11(2), p. 483. (In Russ.).

27. Mokhov, A. and Yavorsky, A., (2020). High-Tech Ethics: Establishment Issues and Development Prospects. *Jurist*, 12, pp. 2–8. (In Russ.).

28. NobelPrize.org. 2021. *The Nobel Prize in Chemistry 2020*. [online] Available at: https://www.nobelprize.org/prizes/chemistry/2020/press-release [Accessed 22.03. 2021].

29. Paix, A., Folkmann, A., Goldman, D., Kulaga, H., Grzelak, M., Rasoloson, D., Paidemarry, S., Green, R., Reed, R. and Seydoux, G., (2017). Precision genome editing using synthesis-dependent repair of Cas9-induced DNA breaks. *Proceedings of the National Academy of Sciences*, 114(50), pp. E10745–E10754.

30. Rebrikov, D., (2021). Human genome editing. *Bulletin of RSMU*, 3, pp. 4–14.

31. Rulten, S. and Grundy, G., (2017). Non-homologous end joining: Common interaction sites and exchange of multiple factors in the DNA repair process. *BioEssays*, 39(3), p. 1600209.

32. Vitelli, V., Galbiati, A., Iannelli, F., Pessina, F., Sharma, S. and d'Adda di Fagagna, F., (2017). Recent Advancements in DNA Damage-Transcription Crosstalk and High-Resolution Mapping of DNA Breaks. *Annual Review of Genomics and Human Genetics*, 18(1), pp. 87–113.

33. Wang, X., Lee, B. and Zha, S., (2020). The recent advances in non-homologous end-joining through the lens of lymphocyte development. *DNA Repair*, 94, p. 102874.

34. You, L., Tong, R., Li, M., Liu, Y., Xue, J. and Lu, Y., (2019). Advancements and Obstacles of CRISPR-Cas9 Technology in Translational Research. *Molecular Therapy — Methods & Clinical Development*, 13, pp. 359–370.

35. Zischewski, J., Fischer, R. and Bortesi, L., (2017). Detection of on-target and off-target mutations generated by CRISPR/Cas9 and other sequence-specific nucleases. *Biotechnology Advances*, 35(1), pp. 95–104.

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On the Issue of Discrimination Based on Genetic Status: Legal Approaches in the Judicial Practice of Foreign States

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Abstract: This paper is devoted to the consideration of legal approaches to discrimination based on genetic status, formulated by the judicial practice of a number of foreign countries: Australia, the USA and Canada. The author notes that the regulatory framework for combating discriminatory practices based on genetic status has developed at the level of international law with the adoption of key documents in the relevant area. The author makes a conclusion about the ways to apply genetic information, which often acts as a "tool" for the implementation of discriminatory practices. As genetic testing becomes more widespread, the challenge will inevitably arise to determine what role genetic information should play in human and social life.

Keywords: discrimination; genetic information; genetic status; human rights; human genome; insurance; employment; judicial practice; legal regulation; international law; "soft" law

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Contents

I. Introduction

Genetic information can be used for discrimination purposes. The results of genetic testing in an outwardly healthy person can show a high risk of developing a disease that will require expensive medical care. Such information may influence the decision on the employment of a candidate for a job or the conditions for concluding an insurance contract with him.

Today it is difficult to talk about the long-term ethical and legal consequences of the gradual «introduction» of genetic testing in the field of employment, insurance, preventive medicine. Nevertheless, cases of discrimination based on genetic status occur in different parts of the world,[1] for example, the Canadian media report cases of discrimination against applicants by insurance companies, regarding the results of testing in terms of the potential for hereditary diseases.[2] Governments of the United States, Australia and a number of European countries have passed legislation to combat genetic discrimination.

[1] National Center for Biotechnology Information (U.S.), GTR: Genetic Testing Registry. Available at: https://www.ncbi.nlm.nih.gov/ [Accessed 25.01.2021].

[2] Several magazines and websites published a story about a teacher in Germany who was denied a full-time job because her father suffered from Huntington's disease, a genetic disorder, and she was at high risk of developing such a disease. The teacher opposed genetic testing and secured employment. The German court ruled that the employer's refusal was discriminatory and stated that the applicant should have the right to work at this place of work indefinitely.

Canada has legislation on human rights, insurance, and privacy to minimize undue discrimination and prevent inappropriate access to or use of personal information, but there is currently no act that provides specific protection against genetic discrimination.

II. Legal Framework at the International Level

Counteracting discrimination based on genetic status has an international legal component. In the 1990s, the Human Genome Project,[3] through which the complete sequence of the human genome was discovered and studied, highlighted the need to find answers to ethical and legal questions related to genetic testing and genetic manipulation. Subsequently, the "Human Genome" project served as the framework for the adoption of a number of international acts, which dealt with the problem of discrimination based on genetic status.

The United Nations Educational, Scientific and Cultural Organization (UNESCO) advocates that all states provide protection against discrimination based on genetic data or genetic characteristics. In 1997, UNESCO adopted the Universal Declaration on the Human Genome and Human Rights,[4] which, together with the desire to protect the human genome from various kinds of manipulations that threaten the life and personal integrity of future generations, aims at preventing genetic discrimination and any use of genetic information. That would be contrary to the principles of protecting human dignity and human rights. What is also worth mentioning is the UNESCO International Declaration on Human Genetic Data,[5] which establishes ethical principles for the application of human genetic data so that such data is «not used for purposes that discriminate in a way that is intended to infringe, or has

[3] Health Canada, Human Genome Project. Available at: https://www.canada.ca/en/health-canada/services/science-research/emerging-technology/biotechnology/about-biotechnology/human-genome-project.html [Accessed 25.01.2021].

[4] Universal Declaration on the Human Genome and Human Rights (adopted on 11.11.1997 at the 29th Session of the UNESCO General Conference).

[5] International Declaration on Human Genetic Data (adopted by the resolution of the General Conference of UNESCO on the Report of Commission III at the 20th Plenary Meeting on October 16, 2003).

the effect of infringing human rights, fundamental freedoms or human dignity of an individual or for purposes that lead to the stigmatization of an individual, a family, a group or communities» (Article 7 of the Declaration). At the same time, it is important to remember that the abovementioned documents refer to the so-called «soft law acts», which contain recommendatory rules.

Within the Council of Europe, most member states have signed, but not ratified, the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine (known as the Oviedo Convention at the place of its signature).[6] States signatories[7] have committed themselves to bringing their legislation in line with the principles set out in the Convention. Article 11 of the Convention prohibits any form of discrimination against a person because of his genetic heritage.

In 2008, Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Genetic Testing for Health Purposes was adopted. This Protocol expanded the provisions of the Convention in a meaningful way. In particular, the document defined the principles of informing and obtaining patient consent, as well as genetic counseling. Among other things, the document contains provisions regarding the protection of privacy and the right to information obtained as a result of genetic testing. To date, only a few states have signed and ratified this protocol.

III. Legislation and Law Enforcement Practice in the Sphere of Discrimination based on Genetic Status: Experience of Foreign Countries

States that have adopted relevant legal acts aimed at combating discrimination based on genetic status use different approaches. One such approach is to impose restrictions on freedom of contract in the field

[6] Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine (ETS N 164).

[7] To date, 35 Council of Europe member states have signed the Convention on Human Rights and Biomedicine, 29 of which have ratified it. The 1997 Convention can be called not only the completion of the codification of bioethical principles, but also the starting point for moving towards much more significant goals. Russia is not involved.

of employment and insurance (Lemmens, 2003), which theoretically could contribute to the emergence of general prohibitions (without a specific field of activity) of discrimination because of genetic status or sectoral legal regulation in this part for insurance companies and employers. In particular, both insurers and employers may be prohibited from requiring an applicant or applicant to undergo genetic testing or provide previous test results. An alternative option is to prohibit the use of test results when making certain decisions that may negatively affect the applicant or applicant (when calculating payments to the insured person or when assigning certain tasks to an employee/applicant).

The second approach is characterized by the adoption of more sophisticated, comprehensive privacy legislation to protect genetic data from unauthorized collection, use and disclosure without the consent of the parties concerned, with a few exceptions. Certain jurisdictions have laws that protect patients' rights and give them broader powers to determine and decide how genetic information may be used and when (Lemmens, 2003).

3.1. Australia

Let us cite as an example the experience of certain foreign jurisdictions. Australian law explicitly prohibits discrimination based on genetic status. In 1992, the Commonwealth of Australia passed the Disability Discrimination Act 1992 containing a similar provision. At the same time, the regulations allow discrimination in relation to the insurance sector where there are sufficient grounds. Insurers have the right to use information on the results of genetic testing, even in the absence of obvious signs of illness, in order to refuse insurance payments or increase insurance premiums in the case of life, income, and travel insurance. However, the legislator emphasizes that the discriminatory attitude must be reasonably justified. The insurers also have a duty to consider all possible measures to reduce the risk of an insured event, including constant medical supervision or surgical intervention. This requirement distinguishes between legitimate (but ethically controversial) discrimination based on genetic status within the scope of applicable law, and unlawful genetic discrimination, which

suggests that the insurer's behavior violates regulations (Rothstein, 2018).

Australian law allows insurers to increase premiums and exclude coverage when a person is at risk of certain diseases, such as cancer, or drop coverage altogether based solely on the results of a genetic test.

As part of genetic testing, human DNA is examined, which contains information about the development and functioning of the human body. DNA modifications can indicate a predisposition to serious diseases such as cystic fibrosis, Huntington's disease, or cancer. Doctors can refer patients for genetic testing if they are likely to inherit certain diseases.

Issues of discriminatory attitudes in the field of insurance have arisen within the Australian legal system, both at the level of case law (*Carter v Boehm (1766) 3 Burr 1905, 1909 (Mansfield LJ*), and at the legislative level (Insurance Contracts Act 1984).[8] In particular, the principle was enshrined according to which the applicant undertakes to disclose to the insurer all known information that is relevant to the insurance contract concluded between them, including genetic information. An important role in this area is also played by industry standards used in relation to the collection of genetic information by insurance companies. It is essential to mention the Investment and Financial Services Association of Australia (IFSA), which is involved in the development of the Genetic Testing Policy.[9]

If we consider the legal framework for regulating nondiscrimination in the field of insurance in a comprehensive manner, it must be noted that it is formed at three levels: federal, state and individual territories. At the federal level, the main acts are identified that affect aspects of discriminatory attitudes in insurance: Sex Discrimination Act 1984, Racial Discrimination Act 1975 and Disability Discrimination Act 1992 cited above. Moreover, the SDA and DDA contain special provisions

[8] Parliament of Australia. Inquiry of the Parliamentary Joint Committee on Corporations and Financial Services. Available at: http://www.aph.gov.au/Parliamentary_Business/Committees/Joint/Corporations_and_Financial_Services/LifeInsurance/Public_Hearings/ [Accessed 25.01.2021].

[9] Parliament of Australia. Inquiry of the Parliamentary Joint Committee on Corporations and Financial Services.

on the admissibility of discrimination in the field of insurance in the presence of certain circumstances (Otlowski et al., 2007). The RDA does not contain such a provision. At the same time, it limits the information that insurers are allowed to use in underwriting applications, to ensure that they receive payments in the event of an insurance case. Thus, insurers cannot discriminate between applicants based on race, although life expectancy for Indigenous Australians is known to be markedly lower than for the European population as a whole.

Regarding the legislation at the state and territory level, in each case it is a separate regulation in the field of insurance and non-discrimination. Not surprisingly, states and territories adopted the provisions of the Disability Discrimination Act 1992 under certain conditions. However, such a reception does not exclude the possibility of conflicts of laws adopted at different levels.

In accordance with the *Australian Mutual Provident Society v Goulden* decision[10] of the High Court of Australia, insurance provisions in anti-discrimination law may be challenged on the grounds that they do not comply with federal law which regulates insurance premiums for insurers as per current guidelines and established practice. In the designated case, the High Court held that a provision prohibiting discrimination because of disability in the provision of goods and services under the Anti-Discrimination Act 1977 is invalid to the extent that it does not comply with the Life Insurance Act 1945. As legislation in this area undergoes permanent change in Australia, claims and complaints about genetic discrimination in insurance by default are included in the Disability Discrimination Act 1992.

In 2001, Dr. Christine Barlow-Stewart and David Keyes published a study that identified 48 cases of discrimination in Australia based on genetic information. The research focused on life, health and income insurance. The applicants argued that the insurers' decisions and actions were inappropriate because the insurers did not have up-to-date information and did not have relevant knowledge about the nature of genetic information and genetic disorders.

[10] Australian Mutual Provident Society v Goulden [1986 160 CLR 330].

Researcher David Keyes noted specific cases of discrimination in insurance based on genetic information. In particular, he presented the story of one applicant who was denied income insurance on the grounds that certain members of his family had been diagnosed with myotonic dystrophy. The insurance company said that the decision to provide insurance depends entirely on the results of genetic testing, which he had to undergo. The applicant passed the test and the result was negative, which enabled him to obtain insurance coverage. The Investment and Financial Services Association of Australia (IFSA) commented on the case, noting that «this situation is unlikely to arise at this time as IFSA members cannot require applicants to undergo mandatory genetic testing» (Barlow-Stewart et al., 2009).

The second case concerned an applicant who agreed to undergo genetic testing to identify mutations causing Charcot-Marie-Tutta disease (CMT). The genetic test showed that the applicant had inherited the genetic mutation that causes CMT. Prior to the testing, no such diagnosis was made to the applicant, since its manifestations were minor. He was subsequently denied coverage due to the results of the designated genetic testing. In the opinion of the IFSA, denying insurance coverage in this case does not contradict the statutory exemption and therefore does not constitute illegal discrimination. If it had been about life insurance rather than income, the applicant most likely would not have received a rejection (Lemke, 2005).

These cases have undoubtedly become a valuable source of information about the ways in which genetic information is used by insurance organizations. In the first case, the insurer apparently misinterpreted the concept of «genetic information», so its decision was not fully correlated with the current Australian «anti-discrimination» legislation. In the second case, the insurer's decision to deny coverage appears to be legitimate because the risks to the company were too high.

Certainly, the cases revealed a number of problems associated with the use of genetic information. On the one hand, allowing the unrestricted use of genetic information in this context is a legitimate concern, as such a permit could trigger the creation of a «genetic underclass» that would be denied access to insurance and other related benefits (Keogh and Otlowski, 2013). In addition, the negative use

of genetic information (expressed in the refusal of the applicant to provide insurance compensation or the refusal to conclude an insurance contract) may not have the best effect on ensuring both individual and public health. On the other hand, a fair position was expressed that it is not necessary to distinguish between genetic and any other medical information in the voluntary insurance market, and a ban on the use of genetic information could negatively affect the viability of the insurance industry.

For more than 15 years, the Australian Government has funded the Genetic Discrimination project, which has reviewed and compiled about 100 claims and complaints from individuals who have suffered discrimination because of genetic status by insurance companies. As a result, a number of recommendations were developed for reforming the insurance system:

1. Human Genetics Commission of Australia, as a matter of priority, should develop procedures to evaluate and recommend whether specific genetic tests are to be used in insurance coverage based on their scientific reliability, relevance and validity.

2. The Investment and Financial Services Association of Australia (IFSA) and the Insurance Council of Australia (ICA) need to develop binding rules for their members to ensure that once the Australian Commission on Human Genetics makes a recommendation for the use of a specific genetic test in underwriting; this test will only be used in accordance with this recommendation. During the transition period, insurers should be allowed to continue to use genetic tests in industry policy until the Australian Commission on Human Genetics makes recommendations for these tests.

3. The Investment and Financial Services Association of Australia (IFSA) must require its members to indicate in their respective insurance applications that not all genetic test results are disclosed and that applicants must be informed.

4. Appropriate amendments should be made to the Insurance Contracts Act 1984 in order to specify in detail the obligation of the insurer to provide written reasons in the event of an unfavorable underwriting decision for the applicant. In cases where such a decision is based on genetic information, including a family history of illness, the

insurer should be required to provide strong and meaningful arguments that support the basis for such a decision.

5. Amendments should also be made to the Disability Discrimination Act 1992 to clarify the nature of the information that the insurer must disclose to the Australian Human Rights Commission and to provide equal opportunities to the parties during the examination of the complaint. Legislation should ensure that the applicant has the right to access to the information disclosed in this way.

6. Expanded powers should be granted to specialized insurance complaint organizations — Financial Industry Complaints Service Ltd (FICS) and Insurance Inquiries and Complaints Ltd (IEC) — to enable these organizations to review underwriting decisions related to the use of genetic information, including family medical history. The inclusion of these provisions should ensure the timely and efficient handling of complaints and applications.

7. With regard to providing confidentiality of genetic information, insurers ought to review their consent forms, including those of the medical authorities, to ensure that they contain sufficient information about the collection, use and disclosure of genetic information to help an individual make an informed decision about applying for and signing the consent form. It should be borne in mind, however, that consent to the collection of genetic information for the purpose of evaluating an insurance claim should not be tied to consent to the use of such information for other purposes.

8. Insurers must protect the public interest under the Privacy Act of 1988 with regard to the practice of collecting genetic information about applicants' genetic relatives for the use in underwriting insurance policies.[11]

World experience and the need to reform the relevant sector pushed Australia to introduce a moratorium on the use of genetic testing results in the consideration of insurance claims from July 2019. By harmonizing the requirements with the legislation of a number of

[11] Parliament of Australia. Inquiry of the Parliamentary Joint Committee on Corporations and Financial Services. [Viewed 25.01.2021]. Available from: http://www.aph.gov.au/Parliamentary_Business/Committees/Joint/Corporations_and_Financial_Services/LifeInsurance/Public_Hearings/.

foreign countries, ordinary Australian citizens were able to receive insurance coverage without the need to disclose adverse test results in the amount of up to 500,000 Australian dollars (life insurance) and 200,000 Australian dollars (health insurance). The coverage limits are quite comparable to those in Switzerland, although significantly lower than those in the UK. The moratorium continues to allow the insured person to disclose favorable genetic test results to prove that genetic diseases and risks of their occurrence in future generations are free. The moratorium will be in effect for 5 years, and an assessment of its effectiveness is planned in 2022.

The relevant Australian practice is formed not only from the legislative regulation of various levels, but also the requirements and standards used in the insurance industry and developed by the professional community on their own. The standards and requirements that are being developed by the professional community are designed to balance the interests of both consumers of insurance services and the insurers themselves. At the same time, professional associations and market participants are obliged to take into account the social consequences of decision-making in the field of ensuring non-discrimination based on genetic status in the field of insurance. Australian model is aimed not only at averting the concerns of applicants, whose insurance could be entirely dependent on favorable or unfavorable results of genetic testing, the development of medical knowledge and genetic research, but also at fulfilling the financial obligations of insurers.

3.2. The United States of America

Notable is the American jurisprudence in the field of combating discrimination based on genetic status. The US Equal Employment Opportunity Commission[12] contributed to the resolution of a dispute related to the filing of a claim against an employer who violated the

[12] The United States Equal Employment Opportunity Commission (EEOC) is the Federal agency that governs and enforces civil rights laws against discrimination in the workplace. The EEOC investigates complaints of discrimination based on race, national origin, religion, gender, age, disability, sexual orientation, gender identity, genetic information, and participation and/or opposition to discriminatory practices.

Genetic Information Nondiscrimination Act 2008. The employer requested a family medical history from its employees and applicants (*EEOC v. BNV Home Care Agency, Inc.*).[13] BNV allegedly demanded that employees and applicants pass the so-called «health assessment» (testing), which included a checklist of 29 diseases such as diabetes, various heart diseases and cancer. In the proposed questionnaire, people were asked to answer «yes» or «no» to the question, whether the employee or someone from his or her family was sick with one or another disease. As stated in the case file, applicants were required to complete such a questionnaire after receiving a conditional job offer, and employees were required to submit an updated questionnaire annually.

The Commission filed a lawsuit on its own behalf and an undefined group of persons, because, in its opinion, the activities of the defendant company grossly violated the requirements of the Genetic Information Nondiscrimination Act. The parties settled the dispute in October 2016. The defendant agreed with the injunction for further violations of the Act. The company mentioned it destroyed all confidential disease information forms received since 2014 and agreed to change the form of the questionnaire in order to comply with the requirements of the US law. The defendant also paid USD 125,000 in damages (this amount was divided equally among the employees).

Another notorious case was the *Lowe v. Atlas Logistics Group,*[14] which confirmed the breadth of application of the Genetic Information Nondiscrimination Act 2008. The circumstances of the case were as follows: the respondent Atlas Logistics provided services for the delivery and storage of products. In 2012, one of the company's employees began to periodically defecate at one of the warehouses where food was stored, thereby harming both the products in the warehouse and the health

[13] EEOC v. BNV Home Care Agency, Inc., No 1:14-cv-05441 (E.D.N.Y., Sep. 17, 2014). Available at: https://www.newyorkemploymentattorneyblog.com/files/2014/09/EEOC_v_BNV_HOME_CARE_AGENCY_14-CV-5441.pdf [Accessed 25.01.2021].

[14] Lowe v. Atlas Logistics Group, No 1:13-CV-2425-AT. (N.D.G., May 5, 2015). Available at: https://www.leagle.com/decision/inadvfdco160219000191 [Accessed 25.01.2021].

of people who could be potential buyers of such products. In order to identify the employee, the company decided to obtain genetic samples from two warehouse workers who were suspected of being involved in this "prank".

The company asked two workers to agree to take cheek swabs, and then hired a forensic laboratory to check if the DNA samples matched the excrement found in the warehouse. Despite the fact that the results of laboratory tests did not confirm the participation of these employees in the "giveaway", rumors of testing spread throughout the company. No wonder that employees filed a lawsuit in federal district court in Georgia, alleging that DNA testing initiated by Atlas violated the Genetic Information Nondiscrimination Act 2008, which prohibits employers from requesting "genetic information" from their employees. Judge Amy Totenberg ruled in favor of the warehouse workers, leaving the issue of damages to a jury. It is curious to note that the jury's verdict in this case was positive for the employees: the jury awarded two workers a whopping $ 2.2 million: $ 475,000 in damages and $ 1.75 million in penalties.

This case was another important testament to the inadmissibility of violating the Genetic Information Nondiscrimination Act 2008, demonstrating the dire consequences of employers' reluctance to act according to its provisions. Regardless of the employer's motive (for example, to identify employee health and safety misconduct), and even if the employer does not act on this information, it is illegal to request or require genetic testing of an employee for genetic information.

3.3. Canada

Canada has come a long way towards its own specialized legislation to prohibit discrimination based on genetic status. Only in 2017 the Genetic Non-Discrimination Act was adopted at the federal level.[15] In 2019, in one of the Canadian courts, the question arose about its unconstitutionality. An important case here is *Canadian Coalition for*

[15] Genetic Non-Discrimination Act (S.C. 2017, c. 3). Available at: https://laws-lois.justice.gc.ca/eng/acts/G-2.5/page-1.html#h-1 [Accessed 25.01.2021].

Genetic Fairness v. Attorney General of Quebec, et al.,[16] in which the provincial Government of Quebec made a prejudicial request to the Quebec Court of Appeal. The question was Is the Genetic Status Non-Discrimination Act (its specific provisions) contrary to the jurisdiction of the Parliament of Canada in criminal law under paragraph 91 (27) of the Constitution Act, 1867? The court unanimously replied "yes", finding that the subject of legislative regulation, which provides for access to genetic testing for medical purposes by preventing unauthorized use of the results by third parties, does not really fit into the framework of criminal law.

During these proceedings, the Canadian court considered critical issues that are likely to shape Canadian jurisprudence in future genetic discrimination cases. The Canadian Coalition for Genetic Fairness (the applicant) argued that the Non-Discrimination Act promotes public health by not preventing people from undergoing genetic testing. Thus, the Act, in her opinion, is the current criminal law, which is under the jurisdiction of the federal government. The Coalition proceeded from the premise that if patients fear that the results of a genetic test will put them at a disadvantage when applying for insurance, they will not take such tests and will not know anything about the possibility of certain diseases. The Attorney General, however, argued that the Non-Discrimination Act relates to the obligation of applicants for insurance to properly inform insurers, which in turn is subject to provincial law. According to the Attorney General, the question of the use of genetic testing by the insurance industry is open to provincial regulators, however, the subject of litigation lies in the area of property and civil rights, which is also part of the provincial jurisdiction.

Canada's legislation on anti-discrimination based on genetic status remains the subject of controversy. However, the Privacy Commissioner of Canada supports the Genetic Non-Discrimination Act, arguing that its purpose is to protect people's privacy with respect to genetic information. In addition, the Act is supported by the Canadian

[16] Canadian Coalition for Genetic Fairness v. Attorney General of Quebec, et al. (38478). Available at: https://www.scc-csc.ca/case-dossier/info/dock-regi-eng.aspx?cas=38478 [Accessed 25.01.2021].

Human Rights Commission, which believes that the document pursues a completely legitimate purpose, prohibiting mandatory genetic testing, unauthorized use and disclosure of its results. I hope that after overcoming the differences, Canada will be able to form its own law enforcement practice in this sphere.

IV. Conclusion

The study of foreign experience in the legal regulation of countering discrimination based on genetic status may be useful in the context of ongoing discussions in the Russian media space on the introduction of genomic certification. A genetic passport is a document based on the analysis of a DNA sample, which contains information about a person's genetic uniqueness. In addition to ensuring the health of future generations, preventing hereditary diseases, the task of ensuring the protection of this information as personal data, preventing its use by state authorities and commercial structures for discriminatory purposes becomes urgent. The legal approaches formulated in foreign law enforcement practice will allow the Russian legislator to ensure a balance of private and public interests when resolving the issue of using information on genetic status in spheres other than healthcare.

Genetic information and the methods of its applicability are already changing the world, the view of human history and the approach to health. It is expected that as genetics is applied to more aspects of our lives, further changes will occur that are not yet imagined. One of the important changes will be the emergence of personalized medicine. If it can help people get treatment specifically tailored to their genetic profiles, this could lead to significant savings in the health care system. As genetic testing becomes more widespread, the challenge will inevitably arise to determine what role genetic information should play in human and social life.

References

1. Barlow-Stewart, K., Taylor, S., Treloar, S., Stranger, M. and Otlowski, M., (2009). Verification of consumers' experiences and perceptions of genetic discrimination and its impact on utilization of genetic testing. *Genetics in Medicine*, 11(3), pp. 193–201.

2. Keogh, L. and Otlowski, M., (2013). Life insurance and genetic test results: a mutation carrier's fight to achieve full cover. *Medical Journal of Australia*, 199(5), pp. 363–366.

3. Lemke, T., (2005). Beyond genetic discrimination. Problems and perspectives of a contested notion. *Genomics, Society and Policy*, 1(3).

4. Lemmens, T., (2003). Genetics and Insurance Discrimination: Comparative Legislative, Regulatory and Policy Development and Canadian Options. *Health Law Journal*, pp. 41–86.

5. Otlowski, M., (2001). Is there scope for lawful genetic discrimination in health insurance in Australia. *Journal of Law & Medicine*, 8, pp. 427–432.

6. Otlowski, M., Taylor, S., Barlowstewart, K., Stranger, M. and Treloar, S., (2007). The Use of Legal Remedies in Australia for Pursuing Allegations of Genetic Discrimination: Findings of an Empirical Study. *International Journal of Discrimination and the Law*, 9(1), pp. 3–35.

7. Rothstein, M., (2018). Time to End the Use of Genetic Test Results in Life Insurance Underwriting. *Journal of Law, Medicine & Ethics*, 46(3), pp. 794–801.

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BOOK REVIEW

Revisiting the Regulation of Human Fertilisation and Embryology (ed. by Kirsty Horsey). Routledge, 2015

Review by Maxim A. Belyaev
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The United Kingdom is at the forefront of developments in human reproductive technologies. This country can be justly proud of its record not only in pioneering new techniques for alleviating infertility or conducting research of serious diseases, but also in their effective regulatory oversight. Medical and scientific breakthroughs and public confidence in them based on clear boundaries and controls go hand in hand in this area. The Department of Health undertook a public consultation exercise in 2005 on possible changes to update the law and regulation relating to human reproductive technologies. That was the part of the review intended to ensure that the law remained fit for the purpose in the early 21st century. The consultation involved a succession of reports, reviews, studies and surveys taking account of the rise of new technologies, international developments, and possible changes in public attitudes since the Human Fertilisation and Embryology Act 1990 came into force. A summary of the consultation comments was published in March 2006. The Government carefully considered a full range of viewpoints, suggestions and proposals, many of which had fundamental social, legal and ethical aspects.

As a general result of balancing the competing claims of reproductive liberty and responsibility, patient safety, child welfare, professional autonomy and public accountability, the Human Fertilization and Embryology Act 2008 (hereafter 'HFE Act') was enacted. The book under review critically considers recent developments in the human fertilization legislation, asking whether the HFE Act has achieved

its stated aim of being fit for purpose. Bringing together a range of international experts, the book evaluates the risks and challenges emerging from both established and existing technologies and techniques in the field of human fertilisation and embryology, as well as offering valuable insights into the social and regulatory challenges that lie ahead.

In Chapter 1, Kirsty Horsey notices that advancements in assisted reproductive technologies (hereafter 'ART') since 1978 have opened up a world of possibilities for infertile heterosexual couples, same-sex couples and even single women and men to have children they desire. Scientific offshoots of these technologies continue to be researched, which often leads to new or more effective forms of treatments. However, because researchers and fertility specialists work with the material of human life and the formation of families is a battleground for conflicting versions of social expectations and beliefs, social, moral and ethical considerations are inevitably raised. The law in this area has a difficult task-it must manage ethical expectations against the progress of science and the goal of creating families for those who need assistance. The law is made by parliamentarians who may seek to shape the social meaning attributed to the technologies at hand, or to prescribe the circumstances in which they believe they should be used. It must, therefore, be kept under review at all times, to ensure the law continues to facilitate family formation while offering protections of rights for the parties concerned, as well as not hindering scientific progress. The Chapter then goes on to consider some of the perceived flaws with that original legislation, despite its initial success and rightful description as a legal landmark and a triumph for progress over conservatism. It then considers the changes made to the law in 2008 and whether they adequately, if at all, address the issues arising from the ART and embryology in the twenty-first century.

The reviewed book represents a snapshot of opinions on various aspects of the HFE Act and comparative legislation, analysing and considering whether its provisions go far enough and meet the aim of bringing and keeping the law up to date. It considers the revised 'welfare of the child' clause (Blyth, Chapter 2) that stipulates that clinics must consider the welfare of any putative child before offering any fertility

treatment. The clause has always been contentious since its introduction in 1990. Nevertheless, the Act has provoked a great deal of heated debate in Parliament and in the press, largely due to the proposed removal of the provision requiring clinics to consider the putative child's 'need for a father' as part of the child's welfare assessment, and replace it with a consideration of children's need 'for supportive parenting'. As has been stated and reviewed, it took eight of the 80 hours in total to debate this point when the Act was debated in Parliament (McCandless and Sheldon, 2010), which highlights its controversial nature and the potential cultural significance of the fatherhood notion.

In Chapter 3, Emily Jackson considers a largely unstudied modern phenomenon of 'DIY assisted conception', analyzing not only the law's failure to reach those-not illegal-private arrangements whereby one man may provide sperm for a woman or a couple outside the confines of a licensed clinic and the dangers this may pose, but also the increased dangers of 'internet-assisted conception'. Jackson contends that DIY assisted conception-including the ability to travel abroad to receive treatments that perhaps are not easily available at home-can now be said to 'coexist' with strictly regulated fertility treatments, meaning that regulation both before and after cannot be said to be comprehensive, and then considers whether these gaps in the regulatory framework matter.

Helen Codd (Chapter 4) looks at prisoners' access to fertility treatments. She argues that different questions arise when prisoners and their partners seek access to fertility services, leading to different problems and potentially different legal outcomes, and that these issues are marginalized within the larger debates concerning access, welfare and rights. Up to now, case law and scholarship looking at prisoners' rights in this respect have focused on access to assisted insemination services rather than the IVF. Similarly, there are questions about who makes the decisions when it comes to prisoners seeking fertility services in the sense that it would be politicians rather than clinicians who do this, thus placing them in a category of their own and making decisions in relation to them-and again particularly for female partners-subject to different rules and procedures.

In Chapter 5, Karen Devine considers the idea of 'benefits in kind' in relation to fertility treatments in a novel way. While the IVF with egg-sharing schemes (a reduction in the cost of one's treatment in return for the contribution of ova for someone else) have been around for some time, they are not without controversy. Some define them as a 'win-win' situation, while others express reservation about the potential coerciveness of such an arrangement as well as the potential psychological consequences that might be felt if the sharer fails to conceive while the woman who also used her eggs did. Devine illustrates that while egg sharing provides both parties some benefits, the process may leave non-affluent women what she calls 'doubly disadvantaged'. To counter this, she proposes that the potential for the use and exchange of a different material-umbilical cord blood (UCB) stem cells rather than eggs-might lead to both more equitable access to fertility treatment, whilst also increasing the provision of a much-needed medical resource (UCB stem cells). This would require a necessary merge of the regulatory functions and the oversight of the HFEA and the Human Tissue Authority, an idea seemingly off the agenda at present.

Jeanne Snelling and Colin Gavaghan then consider (Chapter 6), whether the HFE Act is 'fit for purpose' in terms of the regulation of PGD (preimplantation genetic diagnosis). This concept is later mirrored by Isabel Karpin's text (Chapter 12) who compares the Australian PGD regulatory model against that of the UK. Snelling and Gavaghan outline the history of PGD's regulation and contend that the technique was one of the larger driving forces behind the introduction and the form of comprehensive legislation in the first instance (the 1990 Act). They then go on to critically analyze the approach to PGD taken by the HFEA in the years between the two Acts, followed by an analysis of the statutory parameters that govern the provision of the IVF and PGD today. Comparing two examples (the use of PDG to determine rhesus antibody status and to enable sex selection in conditions which are not X-chromosome linked but do have unequal sex incidence, *e.g*. autism), they suggest that the new regulatory regime is no clearer than it was previously. Moreover, they question the role the state has in regulating these kinds of decisions in the first place, rather than patients in conjunction with their doctors.

Laura Riley's investigation (Chapter 7) provides an overview of novel cell reconstruction techniques not yet used in humans that, following Parliamentary assent in February 2015, can now be licensed under the Regulations to the HFE Act to be used in fertility treatments in the UK. 'Maternal spindle transfer' and 'pronuclear transfer' are the two variations of the ordinary IVF currently being researched both in the UK and the US that allow for the embryo to be created without mitochondrial DNA disorders, which may result in children born being affected by an incurable condition. The techniques are considered by many to be controversial as the resulting embryos contain the nuclear genetic material from one woman and mitochondrial DNA from another woman, creating the novel category of 'mitochondrial donor', who has donated an egg for this purpose. This has led to some commentators dubbing the technique the creation of '3-parent babies' (see e.g. Macrae, 2014) or the children who might be born as having 'two mothers'; Riley argues it is wrong to view it this way.

In Chapter 8, Katia Neofytou and Kirsty Horsey, giving a first look at surrogacy in this book, consider failures of the HFE Act to have touched on the sheer number of aspects of the current regulation of surrogacy that need to be addressed. While the Act does bring into line the availability of Parental Orders to same-sex couples and unmarried couples in 'enduring family relationships' with the more automatic allocation of parenthood following the use of other forms of fertility treatment, it has not questioned the assumption that the Parental Order mechanism is the best way to determine legal parenthood following surrogacy arrangements. Examining the way surrogacy arrangements are regulated in Greece and Israel, Neofytou and Horsey consider what alternative methods might be preferable. While these regulatory models have their own imperfections and their own limits, they show the potential for the pre-birth allocation of parenthood and for the state sanctioned surrogacy contracts.

Anita Stuhmcke (Chapter 13) argues that judicial creativity in both jurisdictions (UK and Australian) is borne out of necessity, due to prohibitive domestic policies in the light of internationalized surrogacy. One response to this, she contends, represents the creation of the notion of 'altruistic commerce' (see also Millbank, 2015), a concept that allows

courts in the UK to bridge the gap between profit and morality and judges to retrospectively authorize payments that in technical terms they otherwise ought not to, while in the Australian context the lines between family law and criminal sanctions have been blurred.

In Chapter 9, Eric Blyth and Lucy Frith consider the rights of those born following the use of donated gametes or embryos to access their genetic and biographical histories. The extent to which access should be granted and the extent of the information that may be received have been a major focus of debate and policy in many different jurisdictions. This chapter provides a comparative overview of what is available when over the past few decades professional practice has moved towards favoring disclosure of donor conception and this has in many instances been mirrored by legal developments. The chapter looks at the similarities and differences between the approaches of different legal regimes and considers the current UK law in this context, highlighting ways in which the law could be improved in order to promote the ability of donor-conceived individuals to discover their genetic and biographical history.

In Chapter 10, Antony Blackburn-Starza considers whether mechanisms for redress, when there is a failure in the provision of a fertility service, could be put on a statutory footing. He contends that although definition and categorization of the harm that might arise in the fertility context might be difficult, this is not a reason to ignore them, as they are obvious harms deeply felt by those affected (and often their families). In a detailed reflection on the nature of fertility treatment-based harms and the kind of normative framework in which actionable damage might be enshrined, he argues for the provision of redress to bring fertility treatments into line with other aspects of medicine and, in general, with contemporary trends in bioethics.

Canada's difficulties in regulating reproduction are the subject of Chapter 11. Pamela White critically analyzes Canada's Assisted Human Reproduction Act 2004, a 'less than perfect law', much of which was struck down by a decision of the Supreme Court of Canada in 2010. The legislation had taken as its inspiration the framework and ideologies of the Human Fertilisation and Embryology Act 1990, and it took a long time to pass this Act. Unfortunately, the Supreme Court felt that the 2004 Act exceeded federal powers under the Canadian Constitution,

raising interesting issues of governance of subjects deemed ethically and politically sensitive. White concludes by looking at future potential directions for legislation in Canada.

Repeating the editor's thought, I would like to notice that the collection of essays in this volume makes a valuable addition to the legal literature. The reviewed book will be of interest to scholars in administrative, medical and family law in general and to assisted reproductive technologies' experts in particular.

References

1. Macrae, F., (2014). Three-parent babies "could be a reality within two years" after report finds controversial IVF techniques are "not unsafe". *The Daily Mail,* 3 June.

2. McCandless, J. and Sheldon, S., (2010). "No father required"? The welfare assessment in the Human Fertilisation and Embryology Act 2008. *Feminist Legal Studies,* 18, p. 201.

3. Millbank, J., (2015). Rethinking "commercial" surrogacy in Australia. *Journal of Bioethical Inquiry,* 12, p. 477.

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