GRATA INTERNATIONAL

THE FEDERAL LAW ‘ON THE BIOMEDICAL CELL PRODUCTS’

The Federal Law No. 180-FZ dated 23 June 2016 'On Biomedical Cell Products' (the 'Law') is aimed at developing the sector of biomedical technologies in Russia.

The Law has been developed with a view of the best international practices and regulates relations in connection with the development, pre-clinical trials, expertise, state registration, clinical trials, production, sale, storage, transportation, use, destruction, import in and export from the Russian Federation of biomedical cell products for the prevention, diagnosing and treatment of diseases (states), pregnancy maintenance and medical rehabilitation of a patient, as well as in connection with the donation of biological material for the production of biomedical cell products.

A biomedical cell product is defined by the Law as a complex consisting of cell line(s) and additives of cell line(s) and additives in combination with the registered medicines for medical use ('medicines') and/or medical products.

The Law provides for the following types of biomedical cell products: autologous, allogeneic and combined.

For the first time such concepts as 'cell line', 'cells differentiation', 'donor of biological material', 'safety of biomedical cell product', and 'efficiency of biomedical cell product' are defined at the legislative level.

The Law establishes, in particular, the following fundamental principles of the activity in the area of biomedical cell products:

- a voluntary and gratuitous nature of biological material donation;
- the inadmissibility of the sale-and-purchase of biological material;
- the inadmissibility of creating a human embryo for the production of biomedical cell products;
- the inadmissibility of using biological material obtained by suspension or interruption of the development of a human embryo or fetus for the development, production and use of biomedical cell products.

1. State Registration of Biomedical Cell Products

Under the Law, the following biomedical cellular products shall be subject for the state registration and on condition of such registration may be produced, sold, used, stored, transported, imported in and exported from the Russian Federation:

- all biomedical cellular products being put into circulation in the Russian Federation for the first time;
- earlier registered biomedical cell products, in case of changing the type of the biomedical cell product, its qualitative and/or quantitative composition (except for the composition of additives), biological and other parameters of cell line(s).

An applicant for state registration of a biomedical cell product can be an organisation that has the rights to the results of pre-clinical trials, clinical trials and/or on the technology of production of the relevant product, or another legal entity so authorised.

The form and procedure for filing an application and documents that comprise the registration file of a biomedical cell product must be approved by the competent federal executive authority.

The competent authority shall carry out the state registration of a biomedical cell product within a period not exceeding 150 business days after the receipt of the registration application with the necessary documents.

The term for the registration may be extended up to 250 business days if the competent authority takes a decision on biomedical re-examination and/or the ethical review of the biomedical cell product.

The state registration of a biomedical cell product is performed upon the results of:

1) biomedical examination of the biomedical cell product performed by the federal state budget institution reporting to the competent authority, and includes the following stages:

   – the first stage involves quality examination of the biomedical cell product as well as examination of the documents for obtaining a permit to conduct clinical trials, except for the product that underwent international multi-centre clinical trials some of which were carried out in Russia;

   – at the second stage, upon the results of clinical trials of the biomedical cell product, the examination of efficiency of the product and expertise of the ration of expected benefits to the possible risk of its use is conducted;

2) ethical review of the clinical trials possibility conducted by the Council on Ethics established according to the procedure established by the competent authority;

3) clinical trials conducted on the basis of a permit issued by the competent authority, subject to the opinion of the Experts Commission of the expert institution on confirmation of the biomedical cell product quality and possibility of its clinical trials and opinion of the Council on Ethics on the same. The period of clinical trials is not taken into account in determining the term of the state registration of a biomedical cell product.

The competent authority may refuse the state registration of a biomedical cell product if the Experts Commission has concluded that the efficiency of the relevant product is not confirmed by the findings received or the risk of harm to human health inflicted by the use of this product exceeds the efficiency of its application.

The Law contains provisions on ‘data exclusivity’ that are similar to those contained in the Federal Law ‘‘On Medicines Circulation’: information on the results of pre-clinical trials and clinical trials of biomedical cell products provided by the applicant for state registration of

the product cannot be used for commercial purposes without the applicant's consent during 6 years from the date of state registration of the biomedical cell product in Russia.

Certificate of the registration of a biomedical cell product if the product is registered in Russia for the first time shall be issued for term of 5 years. Upon expiry of this term, the validity of the registration certificate is extended every 5 years, subject to confirmation of the state registration of the relevant biomedical cell product.

The state registration shall be confirmed upon application of the registration certificate holder based on the results of:

- examination of the ratio of expected benefits to the possible risk of application of the biomedical cell product based on the safety monitoring data on such a product conducted by the registration certificate holder and the Federal Service for Supervision in the Area of Health Care (Roszdravnadzor), and

- examination of the quality of the biomedical cell product conducted in case of changes in the regulatory documents for this product.

An examination of the quality of a biomedical cell product and/or examination of the efficiency thereof and/or examination of the ration of expected benefits to the possible risk of the product use shall be conducted in the event changes to the documents contained in the registration file on the registered biomedical cell product are introduced in respect of:

1) certain information specified in the instructions for the product use;

2) place of the product manufacturing;

3) indicators of quality and/or product quality control methods specified in the regulatory documentation;

4) product shelf life.

2. Clinical Trials

Clinical trials of a biomedical cell product can be arranged by an organization holding the rights to the results of pre-clinical trials, clinical trials of the relevant product and/or to the production technology of the product, or a legal entity authorised by the latter, or an educational institution of higher or advanced education, or a research organization.

Clinical trials shall be conducted in one or more medical institutions accredited by the competent authority according to the procedure established by the Government of the Russian Federation, under an agreement for clinical trials of a biomedical cell product signed between an organisation authorised to conduct such a trial and the relevant medical institution.

One of the material conditions of an agreement for clinical trials shall be the total cost of clinical trials with the indication of the amount to be paid to researchers and co-investigator.

The Law provides for an important rule that in Russia in accordance with its international treaties, and in the absence thereof - on the basis of the principle of reciprocity, the results of clinical trials of biomedical cell products held outside the country shall be recognised and accepted.

A report on the results of clinical trials of a biomedical cell product shall be prepared by the organization engaged in the arrangement of the clinical trial and submitted to the competent authority that issued the permit for the trials, within 3 months from the date of completion, suspension or termination of the trials.

The international multi-centre clinical trials of a biomedical cell product in Russia or post-registration clinical trials shall be conducted on the basis of a separate permit to conduct a clinical trials issued by the competent authority following the results of examination of the product quality, examination of documents for obtaining such a permit and ethical review.

Patients can participate in the clinical trials of a biomedical cell product on a voluntary basis subject to signing thereby or their legal representatives of the patient information leaflet.

Children can participate in the clinical trials as patients only subject to the voluntary consent of their parents given in writing, if such trials are required to treat the disease of the relevant child as established by a decision of the medical council.

The Law provides for the categories of persons who may not be engaged in clinical trials of a biomedical cell product, including orphans and children left without parental care, women during pregnancy, childbirth, and breast-feeding (with certain exceptions), military personnel (with certain exceptions), law enforcement personnel, persons confined, as well as persons remained in custody in the pre-trial detention facilities.

A prerequisite for the patients' participation in clinical trials of a biomedical cell product is conclusion by an organization that received a permit to arrange the clinical trials of the compulsory insurance contract for insurance of the risk of harm to life, health of the patient as a result of the clinical trials.

The insurance contract shall be entered into for a period covering the duration of the clinical trials of a biomedical cell product and not less than one year after the trials' completion.

The amount of the insurance coverage under the insurance contract as the general rule shall be 2 million roubles.

3. Obtaining of Biological Material

Biological material (including biological fluids, tissues, cells) can be obtained from a donor for the production of biomedical cell products, including for the pre-clinical trials and/or clinical trials. The biological material donors shall undergo the medical examinations in order to identify contraindications, which shall be conducted in properly licensed organizations on the basis of an agreement between that organization and the manufacturer of the biomedical cell products at the expense of the latter.

Obtaining of biological material for the production of biomedical cell products in case of an intravital donation is permitted subject to the informed consent in writing of the donor or his/her legal representative, which is entered into the medical records of the donor.

The rules for obtaining biological material for the production of biomedical cell products and transfer thereof to the manufacturer shall be established by the competent authority.

The Law provides for the following cases when obtaining of biological material from deceased (in case of postmortem donation) is not permitted:

1) if during the life, an adult capable person or minor declared fully capable in a statutory procedure, which passed a medical examination (hereinafter - the 'legally capable person'), expressed orally in the presence of witnesses his/her disagreement to the post-mortem donation of biological material and the relevant data was entered into the medical records of the respective person in the specified manner;

2) from a deceased minor, except for those declared fully legallycapable, or from a person recognised incapable in the statutory procedure;

3) if there is neither a consent of a legallycapable person expressed during the life to post-mortem donation of biological material for the production of biomedical cell products nor a consent granted by the spouse or one of his/her close relatives.

4. Production and Sale of Biomedical Cell Products

The Law provides for the duty of the manufacturer to approve the regulations of the production of biomedical cell products, which includes:

1) a list of cell lines, medicines, medical products and additives used indicating the quantity of each;

2) information on the equipment used, description of the process and control methods at all stages of the production of a biomedical cell product.

Production of a biomedical cell product shall be in accordance with the requirements of the regulations and rules of good practice for dealing with biomedical cell products, which must be approved by the competent authority.

Production of counterfeit biomedical cell products (i.e., intentionally accompanied by false information about their composition and/or the manufacturer), as well as in violation of the rules of good practice for dealing with biomedical cell products shall be prohibited.

The Law establishes the restrictions on the sale of biomedical cell products: such products may be sold by manufacturers only to:

- other manufacturers of biomedical cell products;
- scientific organizations, educational institutions for researches;
- organizations engaged in medical activities.

The sale terms for biomedical cell products must be approved by the Government of the Russian Federation.

The primary and secondary packaging of autologous and combined biomedical cell products shall be labelled using the RFID techniques with respect to belonging of the biomedical cell product to a particular patient, according to the procedure prescribed by the competent authority.

Pursuant to the Law, the competent authority shall approve as well:

- a list of information to be indicated on the primary and secondary packaging of cell biomedical products and shipping containers of the product;

- the rules for transportation of biological material, cells to prepare cell lines, cell lines designed for the production of biomedical cell products, and biomedical cell products;

- the requirements for the organization and operation of biobanks as well as the rules for storage of biological material for cell lines preparation, cell lines intended for the production of biomedical cell products.

The Law provides for the obligation to destruct biological material, cells for the preparation of cell lines, cell lines intended for the production of biomedical cell products, and biomedical cell products which were unclaimed.

Falsified or poor-quality biomedical products shall be withdrawn from circulation under a decision of Roszdravnadzor; subsequent destruction of such products shall be based on the decision of the owner of the biomedical cell product and/or decision of Roszdravnadzor, or a court.

Counterfeit biomedical cell products shall be also withdrawn from circulation and destructed, but only upon a court's decision.

The procedure for destruction of falsified, poor-quality and counterfeit biomedical cell products shall be established by the Government of the Russian Federation.

5. Import and Export of Biomedical Cell Products

Biomedical cell products can be imported in Russia provided that:

- they are included in the State Register of biomedical cell products;

- their quality was certified by the manufacturer certificate that confirms the imported products compliance with regulatory documents for each relevant product.

The Law establishes a closed list of legal entities that may import biomedical cell products into Russia ('importers'):

1) the product manufacturer for the purposes of own production;

2) the organization that has the right to the results of pre-clinical trials, clinical trials of the biomedical cell product and/or on the production technology thereof, or authorised legal entity for the state registration of the product;

3) organizations of higher and/or additional education engaged in the arrangement of pre-clinical trials and/or clinical trials of biomedical cell products or conducting such trials, as well as other organizations involved in the arrangement of pre-clinical trials and/or clinical trials or hosting such trials;

4) medical organization and those referred to in paragraphs 1 - 3 above for provision of the life-saving medical care to a particular patient subject to the relevant permit of the competent authority.

A particular batch of unregistered biomedical cell products intended for the state registration (including for biomedical examination, pre-clinical trials and clinical trials) or for provision of the life-saving medical care to a particular patient shall be allowed for importation subject to the permit of the competent authority issued upon the importer's application.

Falsified, poor-quality and counterfeit biomedical cell products are prohibited for importation into Russia.

The procedure for importation of biomedical cell products into Russia shall be established by the Government of the Russian Federation in accordance with international treaties of the Russian Federation and regulatory acts of the Eurasian Economic Union (EAEU), and/or Russian legislation on customs affairs.

6. Application (Use) of Biomedical Cell Products

According to the Law, the self-maintained use of biomedical cell products by patients shall not be allowed.

Medical care with the use of biomedical cell products can be only provided by medical professionals who completed a special advanced training program.

Roszdravnadzor may decide to suspend the use of a biomedical cell product, in particular, if it receives information about side effects not listed in on the instruction for use of the product, serious and unexpected adverse reactions, features of the product interaction with medicines, medical products, food and other biomedical cell products that may pose a threat to human life or health, as well as about inconsistency of data on the efficiency and safety of the biomedical cell product contained in the instructions for use.

The Law establishes the obligation of a manufacturer of a biomedical cell product to compensate for the harm caused to the life or health of citizens as the result of application of the relevant product, if one of the following circumstances is proved:

1) the biomedical cell product has been applied for its intended purpose in accordance with the instructions for use, however, the product is of poor quality, which caused harm to the life or health of citizens;

2) the harm to life or health of citizens has resulted from false information contained in the instructions for use of the product.

The organization where the biomedical cell product is used shall compensate for the harm caused to the life or health of citizens due to the use of such a product, if it is proved that the harm to the life or health of citizens was resulted from the use of this product in violation of the instructions for use.

7. Safety Monitoring and State Control in the Area of Circulation of Biomedical Cell Products

The Law provides for the duties of holders of registration certificates for biomedical cell products, legal entities obtained the permits to conduct clinical trials of biomedical cell products, or other legal entities authorised thereby:

- to provide for reception, accounting of, processing, analysis and storage of statement from entities handling biomedical cell products and state authorities reports on side effects, adverse reactions, serious and unexpected adverse reactions in the application of the biomedical cell products, specifics of their interaction with medicines, medical products, food and other biomedical cell products, idiosyncrasy, as well as on other facts and circumstances that pose a threat to human life or health or affecting the change in the ration of expected benefits to possible risk of the application of biomedical cell products;

- in case of reveal of the relevant information, to take measures on elimination the negative effects of such biomedical cell products, prevention of harm to human life or health, protection of patients from the use of such biomedical cell products, additional collection of data on the efficiency and safety of the relevant biomedical cell products.

In case of violation of these duties, Roszdravnadzor may decide to suspend the use of the relevant biomedical cell product.

State control in the area of biomedical cell products circulation to be performed by Roszdravnadzor includes:

- licensing supervision over the production of biomedical cell products;

- state control over activities in the area of biomedical cell products circulation;

- random control of the quality of biomedical cell products.

Timing of unscheduled inspection of entities engaged in biomedical cell products circulation, as well as prior noticing of legal entities and individual businessmen on the beginning of such inspection shall not require a prior approval by the prosecutor’s office.

The Law enters into force on 1 January 2017, except for certain provisions for which other effective dates are specifically established.

As stated above, in order to implement the Law, the Government of the Russian Federation and the competent authority shall adopt a number of regulatory legal acts.

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Best Regards,

GRATA International Law Firm (Moscow)

Corporate and Commercial Law Department

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What we do:

- advising on the requirements and restriction regarding the import and circulation in Russia and other states of medicines and medical products;
- advising and legal support in participating in public procurement;
- advising on legal compliance of advertising and marketing materials and activities, marking, packing, and labels;
- representing interests in the course of public discussions of the drafts of regulatory legal acts including acts of Eurasian Economic Commission.

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