2020

Regulations of the competition: Development of Polish (CAR/CAR-T) adoptive therapy with the use of genetically modified immunocompetent cells

COMPETITION NUMBER: ABM/2020/4

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Glossary

1) **MRA, Agency –** the Medical Research Agency;
2) **Clinical Trial/Study –** any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of one or more investigational medicinal product(s), and/or to identify any adverse reactions to one or more investigational medicinal product(s) and/or to study absorption, distribution, metabolism and excretion of one or more investigational medicinal product(s) with the object of ascertaining its (their) safety and/or efficacy;
3) **Research study** – a research study within the meaning of Article 4 par. 2 of the Act of 20 July 2018 - Law on Higher Education and Science (Dziennik Ustaw 2020, item 85, as amended) in the field of medical and health sciences or interdisciplinary research involving at least two field of science, at least one of which is the field of medical sciences and health sciences;
4) **Beneficiary –** Applicant who signed the Co-financing Agreement;
5) **GCP –** Good Clinical Practice **–** an international medical, ethical and scientific standard for designing, conducting, documenting and announcing the results of clinical trials involving human subjects. Compliance with this standard ensures the protection of the rights and safety of trial subjects, as well as the reliability of the data obtained;
6) **Competition** – a call for proposals for implementation and financing of Projects, announced and conducted by the Agency;
7) **Consortium Member/Partner –** an entity contributing human, organizational, technical or financial resources to the Project, jointly implementing the Project, on the terms specified in the consortium agreement. The difference between partnership and the transfer of tasks or purchase of services is the joint implementation of the Project, including Project management;
8) **Consortium –** a group of entities referred to in point 1.5.1 of the Regulations, established for the joint implementation of the Project, operating on the basis of a consortium agreement concluded, containing the necessary elements of the consortium agreement indicated in Appendix 5 to the Regulations;
9) **Consortium Leader –** a public higher education institution that offers courses at medical faculty and is founder of a Medical Entity being a part of the Consortium or a research institute referred to in Article 3 of the Act of 30 April 2010 on research institutes (Dziennik Ustaw of 2019, item 1350, as amended). The Consortium Leader acts on its own behalf and

on behalf of and for the Consortium Members based on the authorization/power of attorney it has been granted in the consortium agreement. At the same time, the Consortium Leader must be the sponsor of the clinical trial proposed under the Project;

10) **Non-commercial clinical trial (NCCT) –** any clinical trial in which the owner of the data obtained during the clinical trial is a sponsor who is a university or a federation of entities of the higher education and science system within the meaning of the Act of 20 July 2018 - Law on Higher Education and Science or another entity authorized to confer at least a doctoral degree in accordance with the provisions of this Act, a medical entity referred to in Article 4 par. 1 of the Act of 15 April 2011 on medical activities, (Dziennik Ustaw of 2020, item 295 and item 567), a researcher, a patient organization, an organization of researchers or another natural or legal person or an organizational unit without legal personality whose objective is not to derive profit from conducting or organizing clinical trials or from manufacturing or trading in medicinal products. Data obtained during a non-commercial clinical trial cannot be used to obtain a marketing authorization for a medicinal product, to amend an existing marketing authorization or for marketing purposes;
11) **Medical Entity** – an entity referred to in Article 4 par. 1 of the Act of 15 April 2011 on Medical Activity (Dziennik Ustaw of 2020, item 295, consolidated text);
12) **President –** the President of the Medical Research Agency;
13) **Project –** an undertaking that is the subject of a Grant Application, having a specific financial value, implemented within the established time frames on the basis of an agreement concluded with the MRA;
14) **Council** – Council of the Medical Research Agency;
15) **Regulations** – these Regulations of the competition;
16) **Polish Healthcare Facilities Network –** a group of at least four cooperating Medical Entities, based and operating in the territory of the Republic of Poland;
17) **ICT system –** the system referred to in Article 21 par. 1 of the Act, used for carrying out the procedure of call for proposals;
18) **Adoptive Therapy/CAR/CAR-T Therapy –** a therapy that uses cells of the immune system subjected to activation and modifications aimed at enhancing the recognition of cancer cells and increasing cytotoxicity and then administered to the patient;
19) **URPL** – the Office for Registration of Medicinal Products, Medical Devices and Biocidal Products;
20) **Act –** the Act of 21 February 2019 on the Medical Research Agency (Dziennik Ustaw, item 447 and of 2020, item 567);

21) **Grant Application –** an application for Project implementation and financing submitted in the Competition via the ICT system;
22) **Applicant –** Consortium Leader and Consortium Members/Partners jointly;

1. Background information

The Competition No. ABM/2020/4 is announced by the Medical Research Agency (MRA). The Agency is a state-owned legal person responsible, inter alia, for the development of scientific research in the field of medical sciences and health sciences. MRA is an entity whose task is to support processes contributing to the growth of innovation in the healthcare system. The Agency's operations in the area of financing research projects shall bring tangible benefits to patients, in particular by helping to evaluate which new medical technologies and therapeutic methods should be used to meet healthcare needs of our society and to improve the effectiveness of treatment.
The main objectives set for the Medical Research Agency by the Legislator include promoting the advancement of medical and health sciences and contributing to an increase in innovation in Polish medicine by financing non-commercial clinical trials. Ensuring the constant development of medical sciences and health sciences, by financing research projects, is to contribute not only to the improvement of the effectiveness of treatment, but also to strengthening the potential of Polish scientists in the achievements of medical sciences.

1.1. Legal basis

The Regulations of the competition have been drafted under Article 16 par. 4 of the Act. Pursuant to the Act, the Regulations of the competition set out the terms and procedure for selecting projects recommended for financing. The Regulations of the competition are an instructional document, aiming to provide potential project implementers with all information necessary to apply for financing of research and development projects involving non-commercial clinical trials. The document includes information on the time limits, place and forms of submitting Grant Applications, the template of the application form and documents attached thereto, the template agreement for the implementation and co-financing of the Project, detailed criteria for selecting Projects along with their weight.

Entities implementing research projects in the field of non-commercial clinical trials are required to

comply in particular with the principles set out in the following legal provisions: Legal acts:

- Act of 21 February 2019 on the Medical Research Agency (Dziennik Ustaw of 2019, item 447 and of 2020, item 567);
- Act of 6 September 2001 - Pharmaceutical Law (Dziennik Ustaw of 2020, item 944);
- Act of 5 December 1996 on the Professions of Physician and Dentist (Dziennik Ustaw of 2020, item 514 and 567).

Regulations:

- Regulation of the Minister of Health of 5 September 2019 on state aid and de minimis aid granted via the Medical Research Agency (Dziennik Ustaw of 2019, item 1786);
- Regulation of the Minister of Health of 2 May 2012 on Good Clinical Practice (Dziennik Ustaw of 2012, item 489);
- Regulation of the Minister of Finance of 30 April 2004 on compulsory third party liability insurance of investigators and sponsors. (Dziennik Ustaw No. 101, item 1034 and Dziennik Ustaw No. 101, item 845);
- Regulation of the Minister of Health of 26 April 2012 on inspections of clinical trials (Dziennik Ustaw of 2012, item 477);
- Regulation of the Minister of Health of 30 April 2004 on the method of conducting clinical trials involving minors (Dziennik Ustaw No. 104, item 1108);
- Regulation of the Minister of Health of 12 October 2018 on templates of documents submitted in connection with a clinical trial of a medicinal product and fees for submitting an application for clinical trial commencement. (Dziennik Ustaw of 2018, item 1994);
- Regulation of the Minister of Health of 30 April 2004 on unexpected serious adverse drug reactions (Dziennik Ustaw No. 104, item 1107);
- Regulation of the Minister of Health of 9 November 2015 on the requirements of good manufacturing practice (Dziennik Ustaw of 2019, item 728);
- Regulation of the Minister of Health and Social Welfare of 11 May 1999 on the detailed rules for the appointment and financing as well as the mode of operation of Bioethics Committees (Dziennik Ustaw No. 47, item 480)

1.2. Grounds for the competition

Adoptive therapies (CAR/CAR-T) using the potential of genetically modified immunocompetent cells (T-cells, NK cells, and others) represent an extremely promising therapeutic tool for cancer

patients. So far, oncology has achieved significant successes in the fight against cancer thanks to the use of chemotherapy and radiotherapy, however, in many cases the therapeutic effect is unsatisfactory or temporary. In recent years, adoptive therapy using modified immunocompetent cells (CAR-T) has become an extremely attractive alternative, showing high efficiency in the treatment of patients in the terminal stage of haematological malignancies. This type of therapy seems to be one of the biggest breakthroughs in oncology since the introduction of chemotherapy. At the same time, the potential of adoptive therapies is not limited to blood cancers. Currently, there is an intensive growth of research aimed at using the potential of CAR-T in the treatment of solid tumours, autoimmune diseases and even infectious diseases. Some of the benefits of adoptive CAR/CAR-T therapies include:

- an additional therapeutic option for patients for whom the current standard therapeutic procedures do not bring the expected results,
- the possibility of treating neoplasms that do not respond to chemotherapy, even in palliative patients,
- the possibility of complete recovery of patient from neoplastic disease - lifelong remission,
- the possibility of restoring the patient's efficient functioning in society following one-time treatment,
- faster recovery of patients.

In Poland, the existing potential in the area of therapeutic application of adoptive therapies is not fully utilized and Polish patients do not have access to the currently most promising adoptive therapy. The main reasons for this phenomenon are the very high cost of this type of treatment, but also stringent requirements for medical entities offering this type of therapy.

Although since 2016 there has been a rapid increase in the number of clinical trials in this area and there are currently over 500 clinical trials testing the use of CAR-T cells, a negligible number is conducted in Poland with the participation of Polish patients. The first administration of the registered medicinal product based on CAR-T cells did not take place until January 2020. Therefore, the Medical Research Agency, implementing the statutory goal of its activity, which is to support innovations in health care, has prepared a programme aimed at eliminating obstacles to using the full potential in the field of research and application of adoptive therapies in Poland, such as:

- Insufficient funding for research into therapies that use genetically modified cells of the immune system.
- Insufficient level of maturity of CAR-T Therapy and of scientific knowledge about the side effects of this type of treatment.

- The high price of CAR-T Therapy is related to the high costs of preparing a single batch of the drug produced only for one patient. The cost of the therapy negatively affects its availability for patients.
- Failure to adapt the infrastructure necessary for the production of CAR-T medicinal products and their administration to patients.
- Lack of medical personnel experienced in treating patients with CAR-T preparations.

1.2.1. Principles of Good Clinical Practice

Clinical trials funded by the Medical Research Agency must be carried out in compliance with the principles of Good Clinical Practice (GCP), i.e.:

1. Clinical trials should be conducted on the basis of ethical principles based on the Declaration of Helsinki and in line with GCP (Good Clinical Practice) recommendations and applicable law;
2. Before commencing a clinical trial, potential risks and inconveniences in relation to expected benefits for a trial participant and society should be considered;
3. It should be borne in mind that the rights, safety and well-being of trial participants are an overriding value and are more important than the interests of science and society;
4. The results of non-clinical studies and data obtained from previous clinical trials with the investigational product should sufficiently justify the proposed clinical trial;
5. Clinical trials should be justified from the scientific viewpoint and described in a detailed and clear protocol;
6. A clinical trial should be carried out as per the protocol accepted beforehand by an Bioethics Committee;
7. Medical care should be provided and all medical decisions concerning clinical trial participants should be always taken by a qualified physician,
8. Each of the persons conducting a clinical trial should have relevant qualifications: educational background, training and experience matching the tasks to be performed by this person in the trial;
9. Informed and free consent to participate in a clinical trial should be obtained from each person subjecting to a clinical trial prior to enrolment;
10. All information on a clinical trial should be registered, processed and stored in the manner that enables proper reporting, interpretation and verification;
11. Confidentiality of the data enabling the identification of persons participating in should be

protected and respected in accordance with the applicable provisions on the protection of personal data;

12. The investigational medicinal product should be manufactured, transported and stored as per GMP (Good Manufacturing Practice) requirements. Product use should be consistent with the approved clinical trial protocol;
13. Trials should be conducted with the use systems and procedures that constitute the warranty of quality in every aspect of the trial.

1.3. Objective of the Competition

The Competition aims to have is to have entities based and operating in the territory of the Republic of Poland develop a medical scheme for CAR-T Therapy and to focus the potential of research and treatment units on the intensification of works related to adoptive therapies, which will translate into increasing the availability of this type of treatment for patients in Poland.

The Competition is in line with the **Clinical Research Development Programme**, under which the operation of the Medical Research Agency is to help to increase the number of non-commercial clinical trials conducted to the European average. The intention of the Competition is to ensure proper and smooth financing of non-commercial clinical trials in Poland and to stimulate growth of innovation in the Polish healthcare system.

1.3.1. Mandatory activities to be planned during the Project implementation

During the implementation of the Project, the following obligatory activities should be planned:

1. Development, optimization of the application and improvement of the safety of CAR/CAR-T therapy in the treatment of blood cancers in Poland by developing an infrastructure and team capable of producing and administering CAR/CAR-T cells.
2. Obtaining the appropriate permits and certificates for the production of CAR/CAR-T cells and their use in the treatment of patients (development of the production method).
3. Preparation of the trial protocol and its registration.
4. Implementation of a clinical trial, including the creation of an electronic medical database to measure the clinical effect and safety of the therapy in clinical practice.
5. Conducting scientific activity which will enable the use of CAR/CAR-T CAR/CAR-T Therapy in other indications (e.g. solid tumours, infectious, autoimmune or degenerative

diseases) and innovations in the area of CAR/CAR-T technology.

6. Development and implementation of a training programme for medical personnel involved in the treatment of patients with the use of CAR/CAR-T cells.
7. Establishing a Polish Healthcare Facilities Network capable of managing CAR/CAR-T technology.
8. Project management and administration.

1.4. The amount allocated to the Competition

It is assumed that only one Project with the highest number of points will receive funding. The amount allocated for co-financing the Project selected in the Competition is **PLN 100,000,000.00 (in words: one hundred million zlotys).**

The maximum allowable level of project funding is 100% of the costs of the trial.

The amount of co-financing for a single Project will not exceed PLN 100 million.

1.5. Entities authorized to submit Grant Applications

Only a Consortium may be the applicant in the competition.
The Consortium Leader (who is also a sponsor of a non-commercial clinical trial) may only be a public higher education institution that offers courses at medical faculty and is founder of a Medical Entity being a part of the Consortium or a research institute referred to in Article 3 of the Act of 30 April 2010 on research institutes.
Each member of the Consortium is required to submit a declaration of non-financing and not applying for financing of the tasks covered by the application from public funds from other sources (e.g. National Centre for Research and Development, National Science Centre, National Health Fund).

1.5.1. The Consortium

In order to implement the Project, it is obligatory to establish a Consortium consisting of entities established and operating in the territory of the Republic of Poland, which will jointly implement the

Project on the terms specified in the consortium agreement.

The difference between Consortium Member from a subcontractor is its full participation in the implementation of the Project, including the influence on the management of the Project.

The Competition applies the so-called principle of the **"minimum mandatory composition of the Consortium"**, which must include:

1) The Leader: a public higher education institution that offers courses at medical faculty and is founder of a Medical Entity being a part of the Consortium or a research institute referred to in Article 3 of the Act of 30 April 2010 on research institutes.
2) Partners/Consortium Members (other than the Leader):
    a) at least one Medical Entity responsible for the production of CAR/CAR-T cell preparations in Poland (and possibly administration thereof to patients), whereas this entity may participate in the research work carried out under the Project, and;
    b) at least 3 (three) other Medical Entities not listed in point a), with documented experience in the administration of haematopoietic cells, which will perform procedures related to the administration of CAR/CAR-T cells, providing comprehensive care for patients receiving treatment based on CAR technology. These entities may participate in the research work carried out under the Project, and;
    c) other entity or entities mentioned in Article 17 of the Act, with documented experience in immunology, oncology, molecular biology, preclinical studies

- each of them being a unit of the public finance sector or a research institute within the meaning of the Act of 30 April 2010 on research institutes.

Each of the mentioned Medical Entities forming part of the Consortium that files the Grant Application should have a team, infrastructure and experience in performing haematopoietic cell transplants (at least 50 haematopoietic cell transplants annually in adult patients or 15 transplants annually in paediatric patients). The requirement for the number of transplants will be verified on the basis of data on contracts for the provision of health services concluded by the National Health Fund for 2019 (ICD-9 procedures with codes 41.0 with extensions).

The Consortium must be formed before the submission of the Grant Application. This means that the partners have to conclude a consortium agreement, affixing to it qualified electronic signatures and attach it to the Grant Application. The consortium agreement in a bilingual (Polish-English) version signed by the Leader and all Partners must be attached to the Grant Application. The minimum scope of the consortium/partnership agreement is set out in Appendix 5 to the

Regulations.

In the case of Consortium Members who are entrepreneurs in the scope covered by the financial support granted by the Agency, it may also be necessary, to the extent required by the provisions on state aid, to conclude an additional agreement with the Agency regulating the terms of financing granted to these entrepreneurs.

In justified cases, it is allowed to change or appoint an additional Consortium Member during the Project implementation subject to the written consent of the President of the Medical Research Agency obtained before the amendment to the consortium agreement. The change of the Consortium Member requires that an annex to the co-financing agreement be concluded. Each change of the Consortium Member must meet the principle of the "minimum mandatory composition of the Consortium".

If an additional entity joins the Consortium, the total Project budget is not increased, but funds may be transferred between the tasks and the Consortium Members on the terms specified in the co-financing agreement.

In justified cases it is permissible that during Project implementation the Consortium will use subcontractors other than entities that are the addressees of the Competition, including those based outside the Republic of Poland and operating in the field of adoptive therapies, provided that the intellectual property developed as part of such cooperation will belong to the Leader and that the selection of these entities would take place with full application of separate provisions on public procurement.

1.6. Method of submitting Grant Applications

Grant Applications shall be submitted electronically via the ICT system available at www.abm.gov.pl.

The Grant Application is submitted in English, with the exception of description for the general public, which must be prepared also in Polish.

The language requirements for the Grant Application and its appendixes are specified in the table

below:

Document/Appendix	English language	Polish language
Grant Application	X	
Document confirming the authorization to make a binding decision		X
Consortium agreement signed with a qualified electronic signature by the Leader and all Partners.	X	X
CV of the Principal Investigator	X	
CV of the Project Administration Manager	X	
Draft agreement for conducting the clinical trial (Sponsor, Investigator, Site)	X	X
Other appendices (optional)	X	

The Grant Application should include information relating directly to the evaluation criteria described in chapter 4. Only Grant Applications that are complete and meet all formal requirements specified in the Regulations are accepted for the Competition.

In case of technical problems related to the operation of the ICT system, the President may allow the submission of Grant Applications in a form other than through the ICT system. Information on the change in the method of submitting Grant Applications will be posted on the Agency's website.

1.7. Time limits

Grant Applications must be submitted from **15.07.2020 from 15:00 to 30.09.2020 until 15:00** only in the form of an electronic document via the ICT system available on the Agency's website - www.abm.gov.pl.

The date of submission of the electronic version of the Grant Application in the ICT system is considered to be the date of receipt of the Grant Application.

The Project may start no earlier than on **01.10.2020** and no later than on **01.04.2021.**

The maximum duration of the Project should not exceed 6 years.

2. Grant Application evaluation procedure

The formal evaluation of Grant Applications is performed by the Application Evaluation Team consisting of MRA employees. Information on projects that have passed the formal evaluation and have been submitted for content-related evaluation will be published on the Agency's website. The formal evaluation is performed using the Formal evaluation sheet.

Before sending the Grant Application concerning the Project to experts or during the content-related evaluation, all or part of the Grant Applications may be submitted to:

a) legal analysis, in particular with regard to the extent of state aid in the Project;
b) financial analysis.

The above-mentioned analyses are not mandatory. The decision to submit a project to some or all types of analysis is made by the Head of the Application Evaluation Team.

The content-related evaluation is carried out by checking the substantive criteria discussed in section 3.2, i.e. by assessing the Grant Application in terms of meeting:

- statutory criteria
- specific criteria
- bonus criteria

A Grant Application may receive a maximum of **260** points, of which:
- **130** points for statutory criteria;
- Specific criteria are evaluated on a ***meets - does not meet*** basis;
- **130** points for bonus criteria.

Evaluation with the use of statutory criteria is carried out by awarding points from the pool assigned to a given criterion in the form of integers (without fractional parts). If the Project meets a bonus criterion, it receives the number of points specified for the given criterion. If the Project does not meet the given criterion, it receives 0 points.

The evaluation of a Grant Application is considered **positive** if:
- both evaluators awarded at least 50% of points for meeting all the statutory criteria and 50% of points for each individual statutory criterion and
- both evaluators assessed that it meets all the specific criteria.

Grant Application is assessed by two evaluating experts. The evaluator records on the Grant Application Content-related Evaluation Sheet the fact that the Project meets or does not meet the statutory, specific and bonus criteria and records the points obtained by the Project in the individual scoring criteria.

In the event of a discrepancy in the evaluations (e.g. one of the evaluators awarded less than 50% of the total number of points or 50% of the number of points for any statutory criterion), the Grant Application is referred for a third evaluation by another expert. In such a situation, two concurrent evaluations of the evaluating experts constitute the results of the evaluation of the Grant Application.

Based on the number of points included in the Content-related Evaluation Sheets, a ranking list of Grant Applications submitted in the Competition is drafted. The place on the ranking list is determined by the arithmetic mean of the total number of points awarded by two evaluating experts, and Grant Applications are ranked according to the number of points obtained: from the highest to the lowest. In the event that two or more applications obtain the same number of points, the order in the ranking list is determined by the higher total point value awarded under the statutory criteria in the criteria: *scientific value of the project* and *innovative character of the project*.

A recommendation for co-financing will be awarded to one Grant Application with a positive evaluation (in terms of statutory as well as specific and bonus criteria), which obtained the highest number of points calculated as the arithmetic mean of the total number of points awarded by two evaluating experts.

The Grant Application referred to above will be obligatorily submitted for financial analysis, if it has not been carried out earlier. If the Grant Application receives funding, the Applicant shall introduce to the Grant Application all the guidelines and changes indicated as a priority - primarily in the field of financial analysis, and the possibility of concluding a co-financing agreement is dependent on their inclusion by the Applicant.

Applicants are informed in writing about the results of the Competition by means of information addressed to the Consortium Leader.

3. Grant Application evaluation criteria

Each Grant Application submitted during the call for proposals is subject to evaluation, unless it has been withdrawn by the Applicant.
Evaluation of the Grant Application consists in verifying whether the project meets the Formal Criteria and in assessing the Content-related Criteria, including:

- statutory criteria;
- specific criteria;
- bonus criteria.

3.1. Formal criteria

The formal evaluation is performed using the *Grant Application Formal Evaluation Sheet*, a template of which is attached as Appendix 3 to the Regulations. In the case of formal criteria that must be supplemented, the President requests that they be supplemented within 7 days or else the Grant Application will be disregarded. The Applicant may supplement or correct the Grant Application only to the extent indicated by the President, i.e. may not introduce changes other than those indicated in the request.

During the formal evaluation, the following criteria are verified:

1) **Was the Grant Application submitted in an appropriate form and within the required time limit via the ICT system? (YES/NO)**

It is verified whether the Grant Application was submitted between 15.07.2020 from 15:00 to

30.09.2020 until 15:00 in the form of an electronic document via the ICT system available on the Agency's website, i.e. www.abm.gov.com. The date of submission of the electronic version of the Grant Application in the ICT system is considered to be the date of receipt of the Grant Application.

Obligatory criterion (the criterion must be met for the application to be eligible for funding). Failure to meet the criterion results in a negative formal evaluation of the Grant Application and its rejection. This criterion **cannot** be supplemented.

2) **Were the conditions met for participation in the Competition, as specified in the Regulations in points 1.5 and 1.5.1, regarding the composition of the Consortium - including the designated Consortium Leader (This criterion cannot be supplemented)? (YES/NO)**

The criterion will be assessed on the basis of the verification of the **minimum mandatory composition of the Consortium**, including the proper selection of the Consortium Leader pursuant to the provisions of point 1.5 of the Regulations.

Obligatory criterion (the criterion must be met for the application to be eligible for funding). Failure to meet the criterion results in a negative formal evaluation of the Application and its rejection. This criterion **cannot** be supplemented.

3) **Did the Leader and Partners declare that they had not received or applied for public funding from other sources for the tasks covered by the Grant Application (e.g. from the National Centre for Research and Development, National Science Centre, National Health Fund)? (YES/NO)**

The Applicant is required to submit a declaration that it has not received or applied for public funding from other sources for the tasks covered by the Grant Application (e.g. from the National Centre for Research and Development, National Science Centre, National Health Fund, etc.) The Applicant's verification will be carried out in accordance with the provisions of the Public Finance Act (Dziennik Ustaw of 2019, item 869, as amended). Such a declaration should be included obligatorily in the Grant Application and in the provisions of the consortium agreement, which is a mandatory appendix to the Grant Application.

Obligatory criterion (the criterion must be met for the application to be eligible for funding). Failure

to meet the criterion results in a negative formal evaluation of the Grant Application and its rejection. This criterion **can** be supplemented.

4) **Has the Grant Application been completed in accordance with the language requirements specified in the Regulations? (YES/NO)**

In accordance with the Regulations of the Competition, the Grant Application must be submitted in accordance with the language requirements specified in the table in section 1.6. Method of submitting Grant Applications.

Obligatory criterion (the criterion must be met for the application to be eligible for funding). Failure to meet the criterion results in a negative formal evaluation of the Grant Application and its rejection. This criterion **cannot** be supplemented.

5) **Have all the fields of the Grant Application been filled in correctly? (YES/NO)**

It is required to fill in all the fields of the Grant Application and attach a complete set of required appendices. The Grant Application should include information relating directly to the evaluation criteria. Only Grant Applications that are complete and meet all requirements specified in the Regulations are accepted for participation in the Competition.

Obligatory criterion (the criterion must be met for the application to be eligible for funding). Failure to meet the criterion results in a negative formal evaluation of the Grant Application and its rejection. This criterion **cannot** be supplemented.

6) **Did the Applicant provide for the monitoring of mandatory indicators for the Competition and whether their value is greater than "zero":**

- Number of non-commercial clinical trials registered as a result of the Project;

- Number of people covered by the trial (size of the population covered by the intervention)

- Number of Medical Entities where the clinical trial is going to be conducted?

(YES/NO)

Obligatory criterion (the criterion must be met for the application to be eligible for funding). Failure to meet the criterion results in a negative formal evaluation of the Grant Application and its rejection. This criterion **cannot** be supplemented.

7) **Has the Applicant attached the required appendices to the Grant Application? (YES/NO)**

The required appendices include:

- Document confirming the authorization to make a binding decision,
- Consortium agreement signed with a qualified electronic signature by the Leader and all Partners, containing the required provisions indicated in Appendix 5 to the Regulations - Minimum scope of regulations of the consortium agreement,
- CV of the Principal Investigator,
- CV of the Project Administration Manager.

Obligatory criterion (the criterion must be met for the application to be eligible for funding). Failure to meet the criterion results in a negative formal evaluation of the Grant Application and its rejection. This criterion **can** be supplemented.

8) **The Grant Application assumes the start of the Project no earlier than on 01.10.2020 and no later than on 01.04.2021. (YES/NO)**

Obligatory criterion (the criterion must be met for the application to be eligible for funding). Failure to meet the criterion results in a negative formal evaluation of the Grant Application and its rejection. This criterion **can** be supplemented.

9) **The maximum duration of the Project does not exceed 6 years. (YES/NO)**

Obligatory criterion (the criterion must be met for the application to be eligible for funding). Failure to meet the criterion results in a negative formal evaluation of the Grant Application and its rejection. This criterion **can** be supplemented.

10) **Does the Project provide for the implementation of a non-commercial clinical trial in at least one the areas listed below:**

- haematology,
- oncology,
- immuno-oncology,
- CAR/CAR-T adoptive therapy?
  (YES/NO)

Obligatory criterion (the criterion must be met for the application to be eligible for funding). The criterion will be verified on the basis of the descriptions contained in part II.B. of the Grant Application. Failure to meet the criterion results in a negative formal evaluation of the Grant Application and its rejection. This criterion **cannot** be supplemented.

11) **Does the consortium agreement cover the minimum scope of regulations specified in Appendix 5 to the Regulations? (YES/NO)**

Obligatory criterion (the criterion must be met for the application to be eligible for funding). Failure to meet the criterion results in a negative formal evaluation of the Grant Application and its rejection. This criterion **can** be supplemented.

3.2. Content-related criteria

Each Project is subject to content-related evaluation, unless it has been withdrawn by the Applicant or disregarded due to failure to meet formal requirements. The content-related evaluation consists in verifying whether the Project meets:

- statutory criteria,
- specific criteria,
- bonus criteria.

The content-related evaluation is performed using the *Grant Application Content-Related Evaluation Sheet*, a template of which is attached as Appendix 4 to the Regulations.

3.2.1. Statutory criteria

The criteria listed below have been set out in the Act. Pursuant to Article 16 par. 3 of the Act, under Project selection procedure, the following criteria are assessed:

1. Scientific value of the project – from 0 to 20 points

Evaluation of the above Criterion should assume the evaluation of the following components making up the overall evaluation:

- The objective of the research (accuracy of definition of the scientific problem, quality of presentation of the state-of-the-art - (state of the research) based on the current knowledge. Under this point, the evaluation will cover primarily the main subject of the Project leading to the registration a Non-commercial clinical trial.

Number of points: 0-5

- Correctness of selection of research methods and tools in the design of the clinical trial, including the sample size, availability of patients, defining the endpoints in the trial. Also the presented initial results that confirm validity of the proposed Project shall be assessed.

Number of points: 0-5

- Correctness of task planning and division of work between Consortium Members in the context of the intended objective of the Project. The way the tasks were planned within the Project and assigned to the Partners, transparency of the schedule of the planned works and consistency of those elements with the budget shall be assessed.

Number of points: 0-5

- The final result of the proposed Project, that has to be defined precisely. It shall be assessed whether the assumed results of the research work are feasible in the context of the assumed schedule and budget. The description of identified and precisely defined risk elements (physical, technical, psychological, social, legal, regulatory or economic) related to both the research programme and the preparation and conduct of clinical trials will also be assessed.

Number of points: 0-5

The partial evaluation criteria will be summed up and will contribute to the evaluation of the whole criterion. The total evaluation is made on a scale from 0 to 20, and the number of points awarded means that the Project meets the criterion to the extent:

- 20 – excellent
- 15–19 – very good
- **10–14** – good

- 8–9 – average
- 5–8 – poor
- 0–4 – insufficient

The point threshold required for positive evaluation of a Project under this criterion is **10** points.

2. Criterion: Impact of the Project on the improvement of the health of citizens, taking into account the need to: (TOTAL of maximum 40 points)

1) save life and obtain a full recovery (from 0 to 10 points),
2) save life and obtain health improvement (from 0 to 10 points),
3) prevent premature death (from 0 to 10 points),
4) improve the quality of life (from 0 to 10 points);

Under this criterion, the impact of the proposed Project on the improvement of citizens' health will be assessed if the results of the proposed Project are introduced into clinical practice. Wherein

Sub-criterion 1 (save life and obtain full recovery) should be understood as innovative medicinal products, medical devices or procedures allowing to provide assistance to patients in emergencies leading to death, and the application of which allows to restore their full health.

Sub-criterion 2 (save life and obtain health improvement) should be understood as innovative medicinal products, medical devices or procedures allowing to provide assistance to patients in emergencies leading to death, and the application of which allows for a substantial improvement in the patient's health.

Sub-criterion 3 (prevent premature death) should be understood as innovative medicinal products, medical devices or procedures that allow for a substantial improvement in the health condition of a patient whose prognosis is poor despite the use of the best drugs or medical procedures currently available.

Sub-criterion 4 (improve the quality of life) should be understood as innovative medicinal products, medical devices or procedures that allow the treatment of diseases that substantially reduce the quality of life of patients, leading to their long-term exclusion from social and professional life.

The evaluation is made on a scale from 0 to 40, and the number of points awarded means that the Project meets the criterion to the extent:

- 40 – excellent
- 35–39 – very good

- **20–34 – good**
- 18–19 – average
- 15–18 – poor
- 0–14 – insufficient

The point threshold required for positive evaluation of a Project under this criterion is **20** points.
The criterion is verified on the basis of the entire Grant Application, with particular emphasis on point II.B.

3. Criterion: Innovative character of the Project (from 0 to 20 points);

The Project will be scored taking into account the significance/breakthrough nature of the proposed solution in the context of the current market situation in the country and abroad (compared to competitive solutions).

For the purposes of evaluating this criterion, it is assumed that the innovation is the introduction of a new or significantly improved solution in relation to the currently authorized medicinal products or the method of organizing the therapy.

Within this criterion the following shall be assessed:

- the main subject of the Project, i.e. the development of Polish CAR/CAR-T Therapy by entities based and operating in the territory of the Republic of Poland and its testing in a clinical trial **(from 0 to 10 points)**,
- subject related to research on the use of CAR/CAR-T in new applications, such as the treatment of solid tumours, autoimmune, degenerative, infectious diseases, etc. **(from 0 to 10 points)**.

The evaluation is made on a scale from 0 to 20, and the number of points awarded means that the Project meets the criterion to the extent:

- 20 – excellent
- 15–19 – very good
- **10–14** – good
- 8–9 – average

- 5–8 – poor
- 0–4 – insufficient

The point threshold required for positive evaluation of a Project under this criterion is **10** points.
The criterion is verified on the basis of the entire Grant Application, with particular emphasis on point II.B.

4. Criterion: Expected economic results (from 0 to 20 points);

In particular, the following is subject to evaluation:

- Demonstration and justification of economic benefits that result from the potential use of the outcomes of the Project in medicinal practice in relation to the current costs, including indirect costs for the health care and welfare system. Potential economic benefits resulting from the main subject of the Project, namely development of a CAR/CAR-T therapy, as well as side subjects, namely possible application of therapies of this type in new indications, shall be assessed **(from 0 to 10 points)**.
- The estimated cost of the CAR/CAR-T Therapy under development versus the realistically estimated savings for the budget that such therapy may bring. The Grant Application should include an analysis supported by the number of patients in Poland and Europe who could potentially benefit from the adoptive therapy under development, the cost of current treatment of a given disease entity throughout the patient's life, the likely (but well-estimated and documented) cost of one administration of the CAR/CAR-T Therapy under development **(from 0 to 5 points)**.
- Correct identification and description of possible risks/threats/barriers preventing the achievement of positive economic effects **(from 0 to 5 points)**.

The evaluation is made on a scale from 0 to 20, and the number of points awarded means that the Project meets the criterion to the extent:

- 20 – excellent
- 15–19 – very good
- **10–14** – good
- 8–9 – average
- 5–8 – poor
- 0–4 – insufficient

The point threshold required for positive evaluation of a Project under this criterion is **10** points. The criterion is verified on the basis of the entire Grant Application, with particular emphasis on point II.B.

5. **Criterion: Possibility of using the outcomes of the Project in the healthcare system (from 0 to 20 points);**

The main subject of the Project, understood as the development of CAR/CAR-T Therapy, and additional research subjects assuming the use of CAR/CAR-T in new therapeutic indications, are being assessed, in particular:

- Justification of the demand for the results of the Project on the part of the health care sector, including identification of the disease entity/entities and related problems for the health care system, identification of the target group (of patients), presentation of the quantity and quality of market data constituting the basis for justification **(from 0 to 10 points)**;
- Analysis of the possibility of putting the Project outcomes into practice on the basis of market data **(from 0 to 5 points)**;
- Evaluation of the plan for the transfer of know-how and new technologies resulting from the Project to the health care system based on the analysis of similar cases of treatment involving ATMP-type medicinal products **(from 0 to 5 points)**.

The evaluation is made on a scale from 0 to 20, and the number of points awarded means that the Project meets the criterion to the extent:

- 20 – excellent
- 15–19 – very good
- **10–14** – good
- 8–9 – average
- 5–8 – poor
- 0–5 – insufficient

The point threshold required for positive evaluation of a Project under this criterion is **10** points.

The criterion is verified on the basis of the entire Grant Application, with particular emphasis on point II.B.

6. **Criterion: Consortium participants possessing material and human resources necessary to implement the Project (from 0 to 10 points).**

The evaluation of this criterion will be carried out with particular emphasis on the analysis of the adequacy of the selection of the team composition to the achievement of the Project objectives.

The Applicant should include information about the principal investigator and key team members. These persons should be appropriately selected in the context of the competences necessary to implement the Project. The competence and experience of teams of, for example, doctors and medical staff involved in the medical part, scientists involved in the research and development part, persons responsible for the preparation of a clinical trial or development of procedures, etc. will be assessed.

Evaluation will also consider whether the Leader and Partners have resources enabling organizational preparation for the implementation of the Project, the medical infrastructure that allows to conduct CAR/CAR-T Therapy, access to scientific and research infrastructure (rooms, scientific and research equipment and other equipment necessary for the implementation of the trial, including the pharmacy).

In particular, the following is subject to evaluation:

- scientific achievements of the Principal Investigator (current bibliometric indicators, including the number of citations, H index, total impact factor in the last 5 years before submitting the application),
- professional experience of the Project Administrative Manager,
- managing domestic and foreign research projects,
- awards and distinctions,
- special scientific achievements,
- international cooperation,
- long-term internships abroad (over 3 months).

As part of the evaluation of the criterion, the following aspects will be verified:

- proper selection of the Leader and Partners performing tasks under the Project,
- complementarity of competences of the teams involved in the Project and the resources of the Partners,
- proper selection of Partners for research and development works enabling the optimal use of resources of individual entities.

The Applicant must have all the key human resources at the stage of submitting the Grant Application.
According to Article 20 of the Minister of Health Regulation of 2 May 2012 on Good Clinical Practice, the Sponsor, on the basis of an agreement concluded in writing, may delegate some or all of its obligations or activities specified in the requirements of this regulation to a person or organizational unit conducting contracted clinical trials, called hereinafter "CRO". The conclusion of such an agreement does not release the sponsor from the liability related to the conduct of the clinical trial.

The evaluation is made on a scale from 0 to 10, and the number of points awarded means that the Project meets the criterion to the extent:

- 10 – excellent
- 8–9 – very good
- **5–7 – good**
- 4 – average
- 3 – poor
- 0–3 – insufficient

The point threshold required for positive evaluation of a Project under this criterion is **5** points.

The criterion is verified on the basis of the entire Grant Application, with particular emphasis on points I.A. and II.B.

The statutory criteria are evaluative criteria.

The task of the evaluating expert under the evaluated criterion will be to assign a specific number of points to the Project and to justify her/his decision.

For this Competition it was assumed that the Project could obtain maximum 130 points statutory provisions, but in order to be considered positively assessed, it must obtain at least 50% of the total score and at least 50% of points in each of the above criteria.

3.2.2. Specific criteria

Specific criteria are the criteria that must be met by each submitted Grant Application. Failure to meet

any of the specific criteria means a negative evaluation of the Project. These criteria are not evaluative. They are verified in the 0-1 system by assigning them the status of MEETS/ DOES NOT MEET

1. **Is the Grant Application submitted by the Consortium that meets the requirements set out in points 1.5 and 1.5.1, i.e.:**
   - The Consortium Leader is a public higher education institution that offers courses at medical faculty and is the founder of a Medical Entity being a part of the Consortium or a research institute referred to in Article 3 of the Act of 30 April 2010 on research institutes.
   - Consortium Members (other than the Leader):
     1) at least one Medical Entity responsible for the production in Poland of CAR/CAR-T cell products (and possibly administration thereof to patients), where this entity may participate in the research work carried out under the Project,
     2) at least 3 (three) medical entities with documented experience in the administration of haematopoietic cells which will perform procedures related to the administration of CAR/CAR-T cells, exercising comprehensive care of patients in which a therapy based on CAR technology has been applied. These entities may participate in the research work carried out under the Project,
     3) other entity or entities mentioned in Article 17 of the Act on the Medical Research Agency, with documented experience in immunology, oncology, molecular biology, pre-clinical studies

- each of them being an entity of the public finance sector or a research institute, in terms of the Act of 30 April 2010 on research institutes? - MEETS/ DOES NOT MEET.

The criterion is verified on the basis of the entire Grant Application, with particular emphasis on point I.A.

2. **Each of the Medical Entities forming part of the Consortium that files the Grant Application should have a team, infrastructure and experience in performing haematopoietic cell transplants (at least 50 haematopoietic cell transplants annually in adult patients or 15 transplants annually in paediatric patients).** - MEETS/ DOES NOT MEET.

3. **Each Consortium Member may submit only one Grant Application under the Competition, regardless of whether they act as Consortium Leader or as Partner.** - MEETS/ DOES NOT MEET.

4. **The Project envisages that the entire technological process connected with CAR/CAR-T cells production will take place within the territory of Poland. Production of vectors necessary for the preparation of CAR/CAR-T cells outside Poland is allowed**. - MEETS/ DOES NOT MEET.

5. **The Project envisages that the intellectual property rights to the developed CAR/CAR-T therapy remain the property (non-transferable to any extent) of the Consortium Leader**.- MEETS/ DOES NOT MEET.

6. **The Project envisages that registration of the clinical trial related to CAR/CAR-T therapy developed within the framework of the Project will take place no later than 3 years after commencement of the Project. The clinical trial shall be a multicentre trial**.- MEETS/ DOES NOT MEET.

7. **The Project envisages that at least 150 persons who meet the medical criteria and are entitled to healthcare under the public healthcare system within the territory of the Republic of Poland will be administered the CAR/CAR-T therapy. The number of 150 patients consists of:**
    a) patients who will receive a CAR/CAR-T therapy that is commercially available, financed from the Project budget (this type of administration is possible for the first 3 years of the Project) and
    b) patients included in the Non-commercial clinical trial launched under the Project, who will receive the developed CAR/CAR-T Therapy.

    - MEETS/ DOES NOT MEET

8. **The Project provides at least for the following activities:**

    1) Development, optimization of the application and improvement of the safety of CAR/CAR-T therapy in the treatment of blood cancers in Poland by developing an infrastructure and team capable of producing and administering CAR/CAR-T cells.
    2) Obtaining the appropriate permits and certificates for the production of CAR/CAR-T cells and their use in the treatment of patients (development of the production method).
    3) Preparation of the trial protocol and its registration.
    4) Implementation of a clinical trial, including the creation of an electronic medical

database to measure the clinical effect and safety of the CAR/CAR-T therapy in clinical practice.

5) Conducting scientific activity which will enable the use of CAR/CAR-T CAR/CAR-T Therapy in other indications (e.g. solid tumours, infectious, autoimmune or degenerative diseases) and innovations in the area of CAR/CAR-T technology.

6) Development and implementation of a training programme for medical personnel involved in the treatment of patients with the use of CAR/CAR-T cells.

7) Establishing a Polish Healthcare Facilities Network capable of managing CAR/CAR-T technology.

8) Project management and administration.

- MEETS/ DOES NOT MEET

9. **The process developed within the Polish CAR/CAR-T Therapy should lead to the maximum shortening of the time between apheresis and the delivery and administration of the product to the patient and should not exceed 4 weeks on average**. - MEETS/ DOES NOT MEET

10. **The Project includes a description of the quality control, transportation and cell storage processes, which ensures a high quality and safety of the CAR/CAR-T therapy for the patient**. - MEETS/ DOES NOT MEET

3.2.3. Bonus criteria

The meeting of the bonus criteria is not obligatory, i.e. failure to meet them does not mean that the Grant Application will be rejected. Bonus points are awarded to the Project only if it has been positively assessed based on the statutory criteria and meets all specific criteria; If the Project meets a bonus criterion, it receives the number of points specified for the given criterion.

1. **The person indicated as the Principal Investigator has documented scientific achievements (at least 2 publications in the field of cancer immunotherapy - as the main author, which have been published in the last 5 years in journals from the List of scientific journals and peer-reviewed materials from international conferences with assigned number of points published by the Minister of Science and Higher Education pursuant to Article 267 par. 3 of the Act of 20 July 2018 - Law on Higher**

Education and Science (Dziennik Ustaw, item 1668, as amended) - valid as at the date of submission of the Grant Application - 10 points for each publication (maximum 20 points),

The criterion is verified on the basis of the entire Grant Application, with particular emphasis on the CV of the Principal Investigator.

2. **The Applicant has a documentation confirming it engagement in international scientific cooperation (joint projects/publications) in the area of research in the field of cancer immunotherapy - 10 points,**

   The criterion is verified on the basis of the entire Grant Application, with particular emphasis on points I.A. and I.B of the Grant Application.

3. **The Applicant has proven experience in conducting clinical trials testing Advanced Therapy Medicinal Products (ATMP) - 10 points,**

   The criterion is verified on the basis of the entire Grant Application, with particular emphasis on points I.A. and I.B of the Grant Application.

4. **The project covers the development and conduct of research in at least one additional indication, apart from combating blood cancers, which is obligatory for the Project. For each subsequent therapeutic indication, the Applicant will receive - 10 points (maximum 20 points),**

   The criterion is verified on the basis of the entire Grant Application.

5. **The number of patients included in the Project is greater than that specified in the specific criterion No. 7 - for every 10 additional patients - 10 points (maximum 30 points),**

   The criterion is verified on the basis of the entire Grant Application, with particular emphasis on point II.B of the Grant Application.

6. **The project envisages the creation of a research base (incubator) within the "Core Facility" Consortium, for Polish scientists/international teams with the participation of Polish scientists, in order to carry out research projects aimed at**

development of adoptive therapies - 20 points,

The criterion is verified on the basis of the entire Grant Application, with particular emphasis on the "Process analysis" part of the Grant Application.

7. **The expenses planned for infrastructure constitute less than 25% of the total Project costs - the Project receives 2 points for each one percentage point of reduction in this category of expenses (maximum 20 points).**

   The criterion is verified on the basis of the entire Grant Application, with particular emphasis on the "Process analysis" and "Detailed Budget of the Project" parts of the Grant Application.

4. Rules of Project financing

The list of costs specified in this part of the Regulations is not a closed catalogue, it is of informative nature, and the data contained therein are to facilitate the planning and allocation of costs under the proposed Project.

In accordance with the assumptions of the Competition, 100% of eligible costs related to activities aimed at developing an adoptive therapy using genetically modified immunocompetent CAR/CAR-T cells by entities based and operating in the territory of the Republic of Poland will be financed.

As part of the Project, a maximum of 10 tasks should be planned, while the cost estimate for the entire Project should contain a maximum of 100 budget items.

When planning expenses, the Applicant is particularly obliged to comply with the principle of prohibiting double financing of expenses from public sources and planning expenses in accordance with the principle of rational and effective spending.

Expenses planned under the Project should take into account the amount or percentage limits within the following cost groups:

- research infrastructure costs - not more than 30% of the Project value;
- costs of the procedure for the development and production of CAR/CAR-T Therapy - not more than 65% of the Project value;
- costs of medical procedures related to conducting clinical trials - not more than 35% of the Project value;

- clinical trial insurance costs - not more than 2% of the Project value;
- administrative and project management costs - not more than 5% of the Project value;
- other - costs that have not been assigned to any of the above groups should be classified to this group - not more than 10% of the Project value.

The following tasks must obligatorily be identified in the Project schedule and in the detailed budget of the Project (cost estimate):

- Task 1. Development, optimization of the application and improvement of the safety of CAR/CAR-T therapy in the treatment of blood cancers in Poland by developing an infrastructure and team capable of producing and administering CAR/CAR-T cells.
- Task 2. Obtaining the appropriate permits and certificates for the production of CAR/CAR-T cells and their use in the treatment of patients (development of the production method).
- Task 3. Preparation of the trial protocol and its registration.
- Task 4. Implementation of a clinical trial, including the creation of an electronic medical database to measure the clinical effect and safety of the CAR/CAR-T therapy in clinical practice.
- Task 5. Conducting scientific activity which will enable the use of CAR/CAR-T CAR/CAR-T Therapy in other indications (e.g. solid tumours, infectious, autoimmune or degenerative diseases) and innovations in the area of CAR/CAR-T technology.
- Task 6. Development and implementation of a training programme for medical personnel involved in the treatment of patients with the use of CAR/CAR-T cells.
- Task 7. Establishing a Polish Healthcare Facilities Network capable of managing CAR/CAR-T technology.
- Task 8. Project management and administration.
- Task 9. Other - the Applicant may add only 2 tasks in its own scope (the maximum number of tasks is 10).

4.1. Eligible costs related to remuneration

The costs related to remuneration may be eligible under the Project, as long as they are justified and result from the specific nature of the Project. The Project funds are used to finance the remuneration of:

a) the research team involved in the implementation of the non-commercial clinical trial Project:

- investigator and co-investigators;
- nurses;
- laboratory diagnosticians;
- hospital pharmacy employees.

b) medical and scientific service of a non-commercial clinical trial:

- person responsible for pharmacovigilance;
- trial coordinator;
- trial monitoring and auditing person,
- biostatistician;
- a person responsible for creating clinical trial documentation (medical writing);
- persons responsible for the manufacture and delivery of the investigational medicinal product;
- persons involved in the manufacture of the medicinal product.

c) administrative staff:

- Project Administration Manager and other personnel directly involved in the administrative management of the Project and its settlement;
- personnel responsible for accounting, payroll and legal tasks relating to public procurement.

Involvement in the implementation of tasks or activities under the Project may take place on the basis of:

- employment relationship (full-time or part-time);
- civil law contract;
- task-related bonuses to remuneration.

Expenses related to staff remuneration must be incurred in accordance with national regulations, in particular in accordance with the Act of 26 June 1974 – Labour Code (Dziennik Ustaw of 2019, items 1040, 2245 and 1043).

The eligible components of staff remuneration are, in particular:

- gross salary;
- social insurance premiums paid by the employer
- contributions to the Labour Fund, the Guaranteed Employee Benefits Fund,

contributions to the Company Social Benefits Fund and expenditure on the Employee Pension Plan in accordance with the Act of 20 April 2004 on employee pension plans (Dziennik Ustaw of 2020, item 686, consolidated text);

- bonuses to remuneration (up to 50% of the basic monthly salary of a given employee effective in the month of payment).

Expenditure on remuneration financed from the Project funds is documented:

- in the case of an employment relationship - through the payroll;
- in the case of a civil law contract - through the invoice and acceptance protocol.

4.2. Eligible costs related to research work, medical procedures and services

Eligible costs related to research work, medical procedures and services include:

a) costs of all medical procedures provided for in the clinical trial protocol;
b) costs of diagnostic, laboratory and imaging tests provided for in the clinical trial protocol;
c) costs of the license/purchase/production of preparations necessary for the production of CAR/CAR-T cells;
d) costs of reagents necessary to carry out development work;
e) costs of purchasing and maintaining animal models and model tissues for research;
f) costs of purchasing necessary research equipment, including laboratory equipment;
g) research and laboratories responsible for the production of an ATMP;
h) cost of purchasing the medical equipment necessary to carry out medical procedures provided for in the clinical trial protocol;
i) costs of service and possible repairs of research infrastructure purchased under the Project;
j) hospitalization costs of patients included in the clinical trial;
k) costs of consultations, counselling and outpatient visits of patients during their recruitment to a clinical trial and during the clinical trial itself.

4.3. Eligible costs related to quality systems and costs of registration procedures

a) costs of developing Standard Operating Procedures (SOPs);
b) costs of the feasibility study;
c) costs associated with obtaining the ATMP classification of medicinal products by the Committee for Advanced Therapies (CAT);

d) the cost of scientific advice provided by the European Medicines Agency (EMA);
e) costs of obtaining the Environmental Risk Assessment certificate;
f) costs related to trial registration at the URPL (official fees, costs of preparing dossier required by the URPL);
g) costs of preparation of documentation submitted to the Bioethics Committee, costs of related official fees.

4.4. Other costs

Under the Project the following expenses may be planned:

a) trial preparation expenses, including:

- costs of developing a clinical trial protocol;
- costs of preparing a complete set of documentation for a non-commercial clinical trial;
- costs of engaging a CRO;
- costs of purchasing and running the Case Report Form (eCRF) computer system, biostatistic and other IT programs for Project management;
- costs of developing and implementing a training programme for medical personnel involved in treating patients with the use of CAR/CAR-T cells and costs of preparing teaching materials needed for this purpose;
- clinical trial insurance costs;
- costs of recruiting clinical trial participants;
- costs of expert and advisory services directly related to the trial,
- costs related to disseminating the results of the clinical trial, including costs related to the organization of conferences and costs related to participation in the conference (participation fees, delegation costs);
- internships, training trips only directly related to acquiring knowledge in the field of CAR/CAR-T Therapy;
- Project promotion costs (publications, website maintenance costs);
- medical transport services;
- Internet, courier and postal services;
- costs of running a separate bank account for the purposes of the Project;
- costs of adapting the premises to the needs of scientific research and medical procedures

provided for in the Project.

To be considered eligible, the above types of costs must be planned under the Grant Application, be indispensable for the Project implementation and be incurred during the Project expenditure eligibility period. Detailed conditions of expenditure eligibility will also be specified in the co-financing agreement concerning the Project.

Additionally, as part of budget planning, the Applicant shall take into account the List of the most common costs, specifying the **maximum values of individual costs.** The List is attached as Appendix 6 to these Regulations.

4.5. List of ineligible costs

The following expenses may not be planned under the Project:

- typical office equipment, including desks, chairs, lamps;
- workstation equipment, including laptops, printers;
- projection screens, multimedia projectors;
- printing and photocopying services, not related to the promotion of the Project;
- bank commissions;
- costs of renting and maintaining buildings;
- rewards and bonuses;
- contributions made by employers in accordance with the Act of 27 August 1997 on vocational and social rehabilitation and employment of disabled persons (Dziennik Ustaw of 2018, item 511, as amended), to the State Fund for Rehabilitation of Disabled Persons (PFRON);
- benefits provided by the Company Social Benefits Fund for employees involved in the Project;
- long-service awards and severance pay for employees involved in the Project;
- payment of additional annual remuneration for employees involved in the Project;
- training not related to the function performed under the Project;
- IT systems that are not directly related to therapy development.

4.6. Disbursement method

The financial support granted is paid to the Beneficiary in the form of an advance or reimbursement in the amount specified in the payment schedule.

The disbursement of funds is made to a separate bank account indicated in the co-financing agreement. In the event of a change of the bank account number, the Beneficiary shall to immediately inform the Agency of such change in writing.

As a rule, the disbursement of subsequent instalments may take place only upon presentation of a duly documented settlement of 60% of the previously disbursed instalments of funds. In exceptional and justified situations, the Beneficiary may receive another instalment upon presentation of a relevant application, if no significant irregularities in the Project's implementation have been identified so far.

The disbursement of subsequent instalments depends on the funds at the disposal of the MRA. **Funding the participation of patients from outside Poland in a non-commercial clinical trial from the Project's funds is impermissible.**

It is allowed to modify the annual budgets of the Project, each such modification requires the MRA approval and the introduction of a correction in the Project's Grant Application.

4.7. Settlement rules

The Beneficiary submits periodic reports on the use of funds, including the content-related and financial part, including, among others:

- description of activities undertaken under the Project;
- description of the results achieved in the reporting period;
- a list of accounting documents relating to expenses incurred in the Project in a given reporting period.

Verification of the declared expenses is performed on the basis of the actual progress of the Project implementation in relation to the achievement of the assumed indicators and milestones specified in the Grant Application.

The first report is submitted within 3 months from the date of Project implementation commencement, and if the co-financing agreement is concluded after that date, then from the date

of signing the co-financing agreement. Subsequent reports are submitted every 6 months.
Reports are submitted to the Medical Research Agency via the ICT system, unless the President orders otherwise. If the report is not submitted within the required deadline, the Beneficiary is obliged to update the payment schedule within the deadline set by the President. Failure to adjust the payment schedule appropriately may result in the loss of the right to obtaining the remaining grant amount.
The Beneficiary notified by the Agency about errors or omissions in the submitted report shall rectify them within 14 days from the date of receipt of the request. The Beneficiary's failure to rectify errors or omissions in the report may result in its rejection and withholding of grant payments. If the Project Beneficiary repeatedly makes the same errors in the implementation and settlement of the Project, the President may terminate the co-financing agreement or consider part of the expenditure, in particular those related to the administrative management of the Project, as ineligible. The Agency may make additions or corrections of a clerical or accounting nature to the Report, without the need for their approval by the Beneficiary. The Agency informs the Beneficiary about the scope of introduced corrections and additions.
The Beneficiary shall settle the entire grant amount received in the final report.
The Leader and Partners are required to keep separate accounting records for the Project in a way that allows identification of individual economic operations. Expenses incurred in the Project must be implemented in accordance with the principles of: fair competition, openness and transparency, impartiality and objectivity and in the absence of a conflict of interest in connection with the performance of the Agreement.
The funds received and not used in a given budget year may be used in the next budget year, unless the Agency requests that the Beneficiary return them.
All original accounting documents regarding the costs incurred must be properly described so that their relationship with the implemented Project is visible. The description of the accounting document should include information such as:

a) number of the Agreement;
b) number of the Task under the Project implementation schedule, under which the expenditure was incurred;
c) the amount for the given task;
d) cost category.

The proof of incurring the expense is the issued invoice or other accounting document of equivalent probative value. The decisive factor in qualifying the cost in terms of deadlines is the date of payment.
In the course of settling the Project, the Agency may request all or selected source documents.

The President may, pursuant to Article 22 of the Act, on the basis of an inspection or an analysis of the contents of the periodic report and having consulted the Council, withhold, suspend or terminate financing of the Project.
The Agency has the right to carry out checks of the project documentation, at any time and in any phase or at any stage of the Project implementation as well as within 5 years from the end-date of Project implementation. **The condition for the settlement of the Project is the publication of the final report on the clinical trial in the ICT system.** All costs incurred must be settled within 60 days after the end-date of the Project. If the settlement shows that the grant has not been fully used for eligible expenditure, the Beneficiary shall return this part of the grant to the Agency's bank account, within the time limit specified in the co-financing agreement.

4.8. End of the clinical trial

Each clinical trial should be ended with drawing up the Clinical Study Report, CSR). The report should be prepared according to the structure defined by the guidelines, including ICH GCP (*Good Clinical Practice* E6) principles - a document developed by the International Conference on Harmonization of Good Clinical Practice with an update (Addendum E6 (R1)) and the relevant guidelines of the European Medicines Agency. It is also necessary that the final study report is prepared on the basis of the international code of ethics, which is the Helsinki Declaration, developed by the World Medical Association. The guidelines concerning the Clinical Study Report are also included in the Minister of Health Regulation of 2 May 2012 concerning Good Clinical Practice. The final clinical study report must be prepared no later than 1 year after the end of the clinical trial.
Also, the President of URPL, the Bioethics Committee and researchers/research institutions should be immediately notified about the premature termination of the trial or its suspension. Grounds for such decision should be stated.

4.8.1. Clinical Study Report (CSR)

A Clinical Study Report is a document that describes a single clinical trial. When writing the report, it should be demonstrated that all the trial procedures and objectives described in the trial protocol were carried out as intended. If there are any deviations, they must be explained in detail. The Clinical Study Report should contain information on, inter alia, the purpose and design of the trial, the description of the population, the evaluation of the drug's efficacy and safety profile, and the research methodology applied. The trial results and conclusions should be based on the data from the statistical

analysis. Basically, in the assumptions defining the structure of the document, the principle of the so-called information pyramids is used, which means creating the following sections/modules, starting with: title, abstract, text, tables, figures and case reports, attachments. In the case of attachments and large-format datasets, a detailed reference should be provided to enable the smooth location of the information.

5. Final provisions

After the works of the Application Evaluation Team are completed, a ranking list containing the following data is published on the Agency's website:

- the Applicant's name;
- the average number of points received by the Grant Application;
- the Project title;
- information whether the project is or is not recommended for funding;
- the amount of public funds awarded.

Applications are ranked according to the scores obtained: from the highest to the lowest.

In the event that two or more Grant Applications obtain the same number of points, the order in the ranking list is determined by the higher total point value awarded under the statutory criteria in the criteria: scientific value of the Project and innovative character of the Project.

The Applicant has the right to lodge a protest with the President against the results of the Competition. The procedure and conditions for lodging a protest are specified in Article 19 par. 8-10 of the Act. **In the Competition concerned, the protest must be submitted in a bilingual Polish-English version.**

Submission of a Grant Application for the Project means that the Applicant accepts the Regulations, including the appendices constituting its integral part.

At the same time, the Medical Research Agency reserves the right to:

- change to the Regulations or any document specifying the terms of the Competition to which the Regulations refer. In such a case, the changes are effective from the date indicated in the information on these changes, published on the website of the Medical Research

Agency. Changes may not result in unequal treatment of Applicants, unless they result from generally applicable law;

- annul the Competition in accordance with Article 19 par. 3 of the Act, in particular, in the event of significant changes in the provisions of law affecting the terms of the competition, force majeure events or other cases justified by a relevant decision of the President of the Medical Research Agency.
- refrain from concluding the co-financing agreement until the doubts are clarified, or refuse to conclude it in the event that the MRA has reasonable doubts as to the Applicant's ability to properly spend public funds, including in line with the Project objectives.

The condition for the transfer of funds is the signing of a co-financing agreement. The Applicant undertakes to conclude a co-financing agreement within 30 days from the date of delivery of the information on the results of the Competition on the Project's recommendation for funding. **The Agency stipulates that failure to meet the above-mentioned deadline may result in the withdrawal of the Project's recommendation for co-financing, amendment of the ranking list and refusal to grant financial support.**

In the event of withdrawal from concluding the co-financing agreement, the Agency may decide to recommend the next Project from the ranking list of positively evaluated Grant Applications.

Appendices to the Regulations constituting an integral part thereof:

1. Template Grant Application
2. Template Co-financing Agreement
3. Template Grant Application Formal Evaluation Sheet.
4. Template Grant Application Content-Related Evaluation Sheet.
5. Minimum Scope of Regulation of the Consortium Agreement.
6. List of the most common costs.

APPROVED BY:…….

/SIGNATURE/