

Challenges Facing the European Infrastructure Network for Clinical Research. Perspectives to Bulgaria

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Los retos ante la red europea de infraestructuras en investigación clínica. Perspetivas para Bulgaria

ABSTRACT: Medical research is subject to ethical standards that promote respect for all human beings and protect their health and rights. While scientific research on humans complies with commonly accepted scientific standards, trials on humans are only to be allowed if the expected outcome and the goals set surpass and outweigh the risks to the condition of the participants.

The Community has established a legal framework for a European Research Infrastructure Consortium (ERIC). In November 2013, with a view to strengthening the position of Europe and the member states in the field of clinical research, the European Commission adopted a Decision for setting up a European Clinical Research Infrastructure Network (ECRIN) with the legal form of a European Consortium for Research Infrastructure (ECRIN-ERIC).

The domestic legislation of the Republic of Bulgaria foresees a procedure for obtaining an opinion from the Ethics Committee for Multicentre Trials, thus introducing a substantial change in clinical trials and non-interventional research.

Activities executed within the framework of the European research infrastructure have an ethical dimension and impact clinical trial networks on both national and international level, which is why the ethics committees are of key importance to clinical trial management.

RESUMEN: Las investigaciones médicas están sujetas a estándares éticos centrados en el respeto hacia todos los seres humanos y en la defensa de su salud y derechos. Algunos grupos de sujetos que toman parte en las investigaciones científicas son vulnerables, por lo cual necesitan protección especial. Las investigaciones científicas en seres humanos corresponden a los estándares científicos y la investigación en seres humanos está permitida solo si los resultados esperados y los objetivos son más altos y de mayor importancia en comparación con el riesgo en el estado de salud de los participantes.

La Comunidad creó un marco regulador para la infraestructura de investigación científica europea (ERIC). En noviembre de 2013 la Comisión Europea, con el objetivo de fortalecer la posición de Europa y de los Estados Miembros en el ámbito de las investigaciones clínicas, tomó la decisión de crear la Red Europea de Infraestructuras en Investigación (ECRIN) bajo la forma de Consorcio Europeo para las Infraestructuras de Investigación (ECRIN-ERIC).

El objetivo principal de ECRIN-ERIC es establecer y usar las infraestructuras de investigación, que ayudará para la colaboración internacional en el área de las investigaciones clínicas, de manera que Europa se convierta en un territorio unido para investigaciones clínicas.

En la legislación interna de República de Bulgaria está previsto el procedimiento para la obtención de la opinión del Comité de Ética de Ensayos Multicéntricos para efectuar un cambio significativo en la investigación clínica y en los ensayos sin intervención. Este procedimiento se realiza a base de los decretos que constituyen la Ley de los Productos Farmacéuticos y la Medicina Humana.

Las actividades realizadas dentro del marco de las infraestructuras de investigación europeas tienen aspecto ético e influyen sobre las redes de investigaciones clínicas en plan nacional e internacional, por lo tanto, los Comités de Ética son de mayor importancia en la gestión de las investigaciones clínicas.

KEYWORDS: European Union, regulation, clinical research, Bulgaria

PALABRAS CLAVE: Unión Europea, regulación, investigaciones clínicas, Bulgaria

Scientific research is subject to ethical standards that promote the protection of human rights. Scientific research must necessarily conform to commonly accepted scientific principles and be based on thorough knowledge of scientific literature and other relevant sources of information.

Clinical trials on humans are to be performed only if the significance of the trial and its results are more substantial than the risks for the participant. This is particularly important when the populations comprise healthy volunteers. Medical research is only justifiable provided there is a reasonable likelihood that the populations in which the research is carried out should benefit from the results of the research.



The normative foundation for a legal structure of joint research facilities of Pan-European interest is based on strategic initiatives contributing to the implementation of the “Research Infrastructure” section of the 7th Framework Programme of the European Union (2007 – 2013) and Horizon 2020 –Framework Programme for Research and Innovation (2014 – 2020).

Regulation No 723/2009 of the Council of 25 June 2009 on the Community legal framework set up a consortium for a European Research Infrastructure (ERIC). The ERIC has legal personality and must have its statutory seat in one of its members (a EU country or a country associated with the EU Framework Programme for Research). Its name must include the abbreviation ‘ERIC’. Membership of an ERIC must comprise an EU country and 2 other countries which are either EU countries or associated countries. They may be joined at any stage by other EU countries or associated countries, other countries or specialist inter-governmental organisations.

An ERIC is considered an international body or organisation in the sense of the directives on value-added tax, on excise duties and on public procurement. It is thus exempted from VAT and excise duties and its procurement procedures are outside the scope of the directive on public procurement.

The liability of the members for the debts of the ERIC is, in principle, limited to their respective contributions.

The applicable law is firstly EU law, then the law of the country of the statutory seat or of the country of operation regarding certain safety and technical matters.

In November 2013, the European Commission, expressing a desire to strengthen the position of Europe and the founding members in the field of clinical research worldwide, as well as enhance cross-border cooperation between the member states of the European Union, implemented a decision on setting up the European Clinical Research Infrastructure Network (ECRIN) as a European Research Infrastructure Consortium (ECRIN-ERIC). This decision was based on the community acquis, and in particular on the Treaty on the Functioning of the European Union and Regulation (EC) and Council Regulation (EC) No 723/2009 of 25 June 2009 on the Community legal framework for a European Research Infrastructure Consortium (ERIC), based on a request to the European Commission to establish a European clinical research infrastructure network in the legal form of a consortium for a European research infrastructure of five countries, among which the Federal Republic of Germany, the Kingdom of Spain, the French Republic, the Italian Republic and the Portuguese Republic. Thus a European research infrastructure consortium and a European clinical research infra-

structure network were established, called ECRIN-ERIC, with the French Republic elected by the other four states as a host country to ECRIN-ERIC.

ECRIN-ERIC constitutes a Pan-European distributed clinical research infrastructure aiming to provide advice and services to multinational clinical research in any medical field and for any category of clinical research, observing high scientific, ethical and quality standards. It thus heightens the capacity of the European Union to explore the determinants of various diseases and to develop and optimize the use of diagnostic, prevention and treatment strategies.

The principal task of ECRIN-ERIC is to establish and operate a research infrastructure supporting multinational collaboration in clinical research, so as to make Europe a single area for clinical trials.

ECRIN-ERIC provides information, advice and services to clinical investigators and sponsors of multinational studies, as well as advice to national and European authorities and policymakers. Information, advice and services provided by ECRIN-ERIC, include in particular support to clinical trial management, which contributes to reducing the fragmentation of the health and legislative systems in Europe. Supporting clinical trial management is directly related to submissions to ethics committees and competent authorities, adverse event reporting, study monitoring, data management and support with insurance contracting.

ECRIN-ERIC pursues its principal task on a non-economic basis. However it may carry out limited economic activities, provided that these are closely related to its principal task and do not jeopardise the achievement thereof.

ECRIN-ERIC provides support to multicentre clinical studies involving at least two countries. It is primarily accessible to investigator-initiated clinical research, but is also open to industry sponsored clinical research projects, originating from any country.

ECRIN-ERIC is a distributed infrastructure that establishes a connection between existing national or regional clinical research networks and promotes collaboration and harmonization. It facilitates the adoption of common standards, tools and practices, which reflects on the structuring of the national networks, while simultaneously encouraging the training of the researchers and all other categories of specialists and non-specialists involved in clinical research. ECRIN-ERIC promotes quality, transparency and optimal use of clinical study data, communicating to patients and citizens the challenges and opportunities associated with clinical research.

The activities conducted within the ERIC have an ethical aspect and an impact on the clinical trial networks on a both national and international level, which is why the ethics committees play a key role in clinical trial management.

The ERIC Regulation (Council Regulation (EC) No 723/2009 of 25 June 2009 on the Community legal framework for a European Research Infrastructure Consortium) creates a new EU-level legal instrument for establishing European research infrastructures with legal personalities that are recognized by all member states. In many of the projects included in the roadmap of the European Strategy Forum on Research Infrastructures (ESFRI), the use of the ERIC is introduced as a legal instrument for the implementation and operation of research infrastructures.

Art. 9, para. 1 of the ERIC Regulation foresees a distinction and difference in the treatment of member states, associated states, third countries other than associated countries, and intergovernmental organizations. An ERIC is to have at least three member states as members (Art. 9, para. 2), with the member states jointly holding the majority of voting rights in the assembly of members (Art. 9, para. 3). An ERIC, however, can only be hosted by a member state or an associated state (Art. 8, para. 1). In order to avoid the impossibility of associated states' hosting or becoming members of consortia, an amendment to the ERIC Regulation was proposed. The amendment of the ERIC regulation solely concerns Art. 9, paragraphs 2 and 3, recommending that creating an ERIC requires at least one member state with at least two member states or associated countries. The amendment also concerns the proportionality of the votes in the assembly of members by introducing the option for member states or associated countries to jointly hold the majority of votes in the assembly of members.

On national level, the domestic legislation of the Republic of Bulgaria foresees a procedure for obtaining an opinion from the Ethics Committee for Multicentre Trials in order to introduce a substantial change in clinical trial and non-interventional study. This procedure is implemented pursuant to Art. 130, para. 1 in conjunction with Art. 103, para. 1 and Art. 109, para. 1 of the Medicinal Products in Human Medicine Act. The procedure aims to evaluate the compliance of the planned clinical trial with the norms of good clinical practice, the requirements of the Medicinal Products in Human Medicine Act and Regulation (EC) No. 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use.

The licensing regime that has been introduced on national level provides for performing a documentation evaluation that performs a major change in clinical trial and non-interventional research, with the liable persons being the chief or coordinating investigator and the medicinal product clinical trial sponsor. Legal definitions of the terms "principal investigator" and "coordinating investigator" have been introduced. The "principal investigator" is

the medical doctor or the dentist, designated by the sponsor, who leads the overall execution of the clinical trial in accordance with the approved protocol and good clinical practice guidelines and is responsible for the researchers. The “coordinating researcher” is a researcher appointed to coordinate researchers from different centres participating in a multicentre trial.

Good Clinical Practice (GCP) is the totality of internationally recognized ethical and scientific quality requirements for designing, conducting, recording and reporting clinical trials. In practice, a clinical trial for a medicinal product is any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of one or more investigational medicinal products, and/or to identify any adverse reactions to one or more investigational medicinal products. A clinical trial may aim to study the absorption, distribution, metabolism and excretion of one or more investigational medicinal products with the object of ascertaining their safety and/or efficacy.

Scientific infrastructure links together the three key factors for establishing a dynamic economic model for sustainable development and employment – education, scientific research and innovation. Therefore, the introduction of measures for determining high quality and safety standards for medical products and devices should be regarded as a high priority activity in the field of public health.

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