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Letter to the Editor

The role of the Ethics Committees in the application of the European Regulation No 536/2014

Dear Editor,

The National Report on Clinical Investigation of Medicinal Products in Italy, published by the Italian Medicines Agency (AIFA) in 2014, has since the year 2009 shown an increase in clinical trials funded by the pharmaceutical industry, after a period of stagnation or decline in certain clinical trials[1]. However, clinical trials conducted by non-profit organizations have marked a distinct change, unlike the rest of the european scenario. In Italy, the No 189/2012 law has transferred to AIFA the competences in the field of clinical trials previously assigned to the National Institute of Health, reorganizing at the same time the Ethics Committee network[2]. The reform of the Italian Ethics Committee was inspired by the desire to simplify the application procedures and ethical evaluation as well as the necessity to clarify the roles, areas of expertise and their functioning, also on a territorial basis. The criteria on which the reform of the Ethics Committees was based, are: (1) that a territorial jurisdiction of one or more provinces would be given to each Ethics Committee, so as to respect the parameter of one committee for every million inhabitants, subject to the possibility of providing additional ethics committees, with extensive expertise in one or more Scientific Institutes for Research, Hospitalization and Health Care; (2) that the choice of the committees to be confirmed would take into account each single opinion for the clinical trials of medicines issued over the last three years; (3) that the competence of each committee would be able to handle, besides clinical trials of medicines, every other issue regarding the use of medicines and medical devices, the use of surgical and clinical procedures relating to the study of alimentary products for human beings, generally attributed as required by international practice, to the evaluations of the committees; (4) to ensure the independence of each committee and the absence of hierarchical relationships among the various committees.

The article of Minacori et al[3] "Research Ethics Committees and clinical research in Italy: where are we going?" is a review of the law No 189 of 2012 and the Ministry of Health Decree of February 8 2013 on the functioning of the Ethics Committees in Italy.

However, it must be taken into consideration that the question of the approval procedures of clinical trials is likely to undergo significant changes as a result of the promulgation of the European Regulation No 536/2014 of 16 April 2014 on clinical trials on medicinal products for human use[4], which has repealed Directive 2001/20/EC.

With this Regulation, the European Commission wanted to boost scientific research, recognizing the centralization of the authorization procedure, managed through the EU portal, as a fundamental tool in order to simplify its process.

This new system brings a more precise approach to the risks in clinical trials and is an attempt to meet the requirements of simplification and harmonization that have been reported by almost all stakeholders in the last few years, starting from the adopted legal body, the Regulation[5] (a legal act of the European Union that becomes immediately enforceable as law in all member states simultaneously) in place of the Directive[5] (legislation that establishes a goal that all EU countries must realize, in which each country retains autonomy application). The previous Directive[6] had significantly improved the safety and ethical validity of the experiments carried out in Europe, but had also been heavily criticized for contributing to the decrease in the number of applications for authorization, increased costs in conducting trials and the personnel responsible for clinical research within the pharmaceutical area, the huge growth of unnecessary paperwork and bureaucracy and the lengthening of waiting time in order to obtain opinions and authorizations, especially at a local level. The procedural experience accrued by the European Medicines Agency (EMA) has allowed the modification of the authorization procedure and the role of Member States' competences making the transition from the coordination, which has characterized the role of the European Regulatory authority in relation to each Member State, to a direct responsibility and harmonization.

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The Regulation[4], although it does not directly deal with the role and regulation of the ethics committees, does not shy away from the ethical issues of the trial, because it clearly states that any clinical trial is subject to a scientific and ethical review. This aspect necessarily deals directly with the role of the Ethics Committees of the Member State. The need for ethical review is limited to a local level and will have to comply with the specific rights of the Member State. The timing and procedures for review of the ethics committee must also align with the timing and procedures to assess the application of the authorization of the trial, as required by the Regulation. Therefore no Member State will be able to legislate beyond the general principles of the EU so the more a sponsor is interested in seeking authorization for clinical trials in a given country, the more it will be guaranteed that the body responsible for the validation of the scientific and ethical aspects of the clinical study will be able to give a quick and rigorous scientific response. A natural competition will develop between member states hopefully overcoming all the regional bureaucracy which up to now have produced this large number of ethics committees. It is reasonable to infer that the current regulation in Italy may not be compatible with the set procedures and with the given times of the regulation.

In evaluating the application for authorization by the reporting member state, it is important to take into consideration any risk or inconvenience to the person by introducing the "low-intervention clinical trial" which means a clinical trial fulfilling the following terms: (1) the investigational medicinal products, excluding placebos, are authorized; (2) according to the protocol of the clinical trial, the investigational medicinal products are to be used in accordance with the terms of the marketing authorization, and the use of the investigational medicinal products must be evidence-based and supported by scientific literature already published on the safety and efficacy of the investigational medicinal products in all of the Member States concerned; furthermore, (3) the additional diagnostic or monitoring procedures must not procure more than a marginal added risk or burden to the safety of the subjects compared to normal clinical practice in any Member State concerned.

In conclusion, a significant innovation emerges, which is highlighted in the key points summarized in Table I.

Table I. Main innovations of the European Regulation No 536/2014.

Introduction of the concept of "low-intervention clinical trial"
EU portal for the request of authorization
Coordinated assessment with defined times for the authorization
Compensation for expenses and loss of earnings directly related to the participation in the clinical trial
Duty of information transparency in the area of clinical trials
New rules for the acquisition of consent
Possibility of co-sponsorship
Possibility of inclusion in the protocol of the consent request for a different use of samples collected, from the purposes of the study
The investigator shall archive the content of the clinical trial master file for at least 25 years

The reporting Member State is required to assess the common elements of the trial. All Member states concerned in the evaluation of the trial will involve both the current competent Authority and the Ethics Committee, to perform an integrated activity. The ethical review is conducted by an Ethics Committee in accordance with the law of the member state concerned. The latter can choose freely whether or not to involve the EC, within the applied terms. The involvement of the Ethics Committee by the Commission is only necessary for the evaluation of the local affectivity, which could represent a significant downsizing of the Ethics Committee activity.

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Conflict of Interest

The Authors declare that there are no conflicts of interest.

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