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OPINION PAPER

THE NEW SHAPE OF THE ITALIAN ETHICS COMMITTEES

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ABSTRACT: 2023 promises to be a turning point in the history of Italian ethics committees, both for factors related to the technical and scientific progress typical of recent years and for the regulatory and procedural revolution introduced by the new European legislation. The publication, on February 8th, of four decrees implementing Law 3/2018 certainly clarified many aspects that had been pending for years however many gray areas still remain.

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Impact statement: Provide an overview of the future reorganization of Ethics Committees in Italy.

Key words: *Ethical Committees; decrees; Regulation 536/2014; observational studies; ethics.*

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INTRODUCTION

2023 promises to be a turning point in the history of Italian ethics committees (EC), both for factors related to the technical and scientific progress typical of recent years and for the regulatory and procedural revolution introduced by the new European legislation (1). Since the first formal institution, in 1998, of the Ethics Committees such as "independent bodies, created within a medical or scientific research institution according to interdisciplinary criteria" (2), different organizational models have followed one another.

An important step towards the evolution, also in terms of competences of the ECs, was represented by the Decree of February 8th, 2013, criteria governing the composition and functioning of ethics committees (3). In Article 1 of that Decree ("Definitions and functions of ethics committees"), paragraph 1 states that *"Ethics Committees (...) shall be independent bodies (...) that have the responsibility of guaranteeing the protection of the rights, safety and welfare of persons involved in trials and of providing public assurance of that protection*". In Paragraph 2 it is specified that "*where these are not already attributed to specific bodies, ethics committees may also perform consultative functions in relation to ethical questions associated with scientific and healthcare activities, in order to protect and promote the dignity of the individual. Ethics committees can also propose initiatives for training of healthcare professionals in relation to the sphere of bioethics*". The natural consequence of this new regulatory act was the drastic reduction in the number of ECs in the area: from 243 in 2012 to 91 in 2014 and 90 in 2019 (4) (**Figure 1**). The new evaluation procedure for clinical trials introduced by Regulation 536/2014 has imposed a new profound reorganization. The old procedure, that included the issuing of a single opinion by a coordinating committee and a subsequent formal acceptance/rejection of this opinion by all the other ECs involved, would not have allowed to meet the tight deadlines of the new legislation. Furthermore, the old process was characterized by a reiteration of processes that would go against the Regulation's inspiring principles.

The first step towards the reorganization was ratified with Law 3/2018 (5), which established 43 ethics committees to be maintained in Italy, 3 national

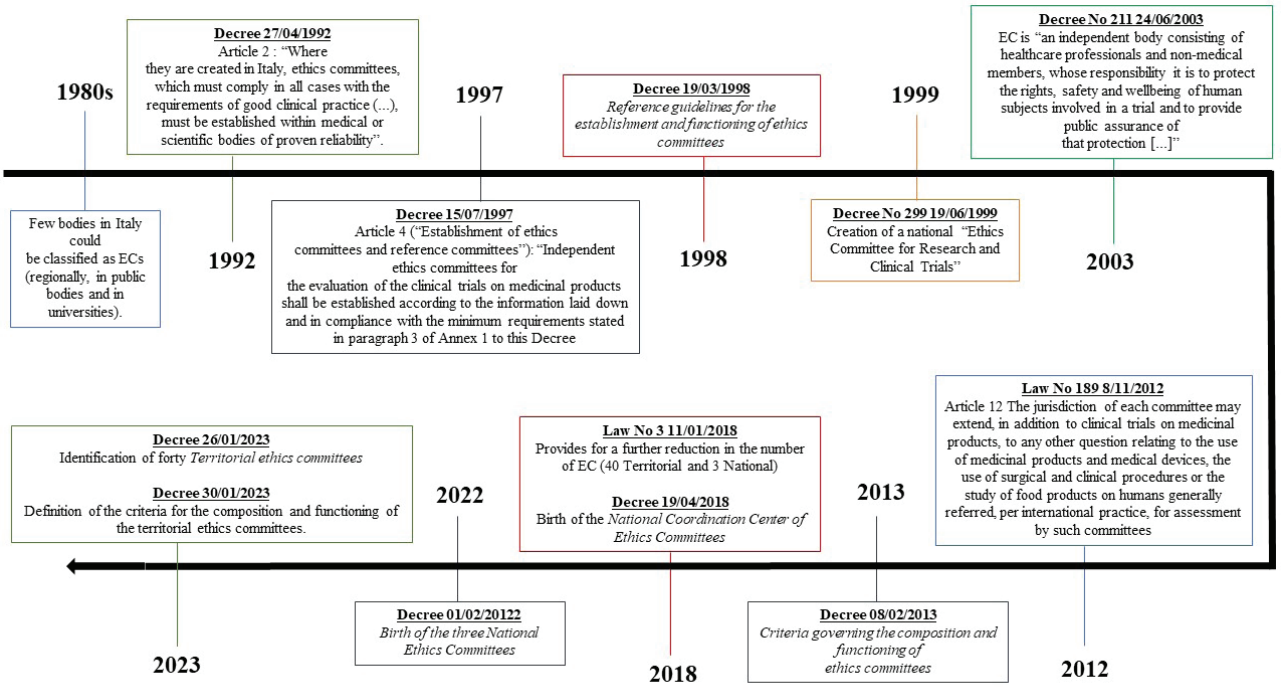

Figure 1. *History if Italian Ethics Committees.*

and 40 territorial. A few months later, a special decree of the Ministry of Health enshrined the birth of the National Coordination Center of Ethics Committees (6), a body with coordination, guidance, and monitoring functions that for a long time has been "a king without a kingdom", as to this day territorial CE is not yet active.

It was necessary to wait another couple of years for the constitution of CEs with a national value (7); one, based at the Istituto Superiore di Sanità (ISS) and immediately operating, has the task to evaluate requests from public research institutes, such as the CNR-Council National Research. The other two, based at Agenzia Italiana del Farmaco (AIFA) and formally active only since the end of January 2023, will evaluate requests relating to studies in the pediatric field and with advanced therapies, respectively.

Despite the formalization of the national EC, many questions remained unanswered for a long time. For example: what should these committees evaluate? Only interventional studies with drug and device or even observational ones? What would have been the limits of jurisdiction between national and territorial EC? Who would evaluate studies other than interventional with drug and device and pharmacological observational, given that only these seemed to be the areas of competence of the territorial EC? What about the assessment of end-of-life requests?

Months went by without having any answers (8) until February 7th 2023, when the long-awaited decrees implementing law 3/2018 have been published (9-12).

IDENTIFICATION, COMPOSITION AND FUNCTIONING OF THE TERRITORIAL EC

Two (9, 10) of the four decrees have clarified tasks and functioning of the territorial EC and have established – after long and debated analyzes with respect to past performance – what would have been the 40 "survived" committees. The idea of also evaluating end-of-life requests, that required special expertise, was dropped due to the sensitivity of the subject the need of new professional figures.

The territorial committees have been entrusted with the evaluation of three types of studies: interventional with drug, interventional with medical device e pharmacological observations. Obviously without going to flow into the areas of competence of the national EC; this means that the territorial committees will never evaluate studies in the pediatric field or contemplating the use of advanced therapy. The promoter will have to choose a single territorial ethics committee that expresses an opinion valid at national level, regardless of the

number and location of the centers involved; the choice, which in the case of interventional studies with drugs can be delegate to AIFA, must be performed ensuring the independence of EC from all the centers that will participate in the study.
Again, with a view to guaranteeing high transparency, the appointment of the members will no longer be up to the General Managers but to the Regions, who will have 120 days (starting from the entry into force of the decree) to proceed with the appointments and set up the committees. Few news, compared to the past, regarding the minimum figures that must be present in these EC and the operating procedures. The components, who will receive a fee equal to 300 euros per session plus any reimbursement of expenses (12), cannot be part of more than one CE at the same time. Still valid is the possibility, in special cases, of also relying on the advice of external professionals; in this case the evaluation must be carried out free of charge and the consultant it should be chosen from special lists/registered maintained by the regions.

EVALUATION OF OTHER TYPES OF STUDIES

Giving the new organizational model, who will be responsible for the assessment of other types of studies that go beyond the competences of national and territorial EC (for example non-pharmacological observational, requests for compassionate use, biological studies)? Also in this case, the decision-making power belongs to the Regions, free to decide whether to entrust these competences of the territorial committees or whether to maintain ancillary committees, defined as "local" (**Figure 2**). The regulatory process, therefore, could slightly differ between different regions.

GRAY AREAS

Despite the relevance of the new regulatory acts, not all doubts have been resolved. The first concerns retrospective pharmacological observational studies that, unlike the prospective ones, will not be able to benefit of a single opinion at national level (13). In addition to the questionability of this choice, it remains unclear who will take charge of the evaluation of such studies, especially if they should fall within the areas of competence of the two national EC under the guidance of AIFA. The same perplexity regarding studies that are not pharmacological observational and non interventional with drug or medical device; also, in this case it seems that an evaluation by multiples committees will be maintained, and it could be a mix between territorial and local EC. Without forgetting the urgent need to open a dialogue with the Italian privacy guarantor, to resolve the delicate problem of retrospective studies on deceased subjects (14).

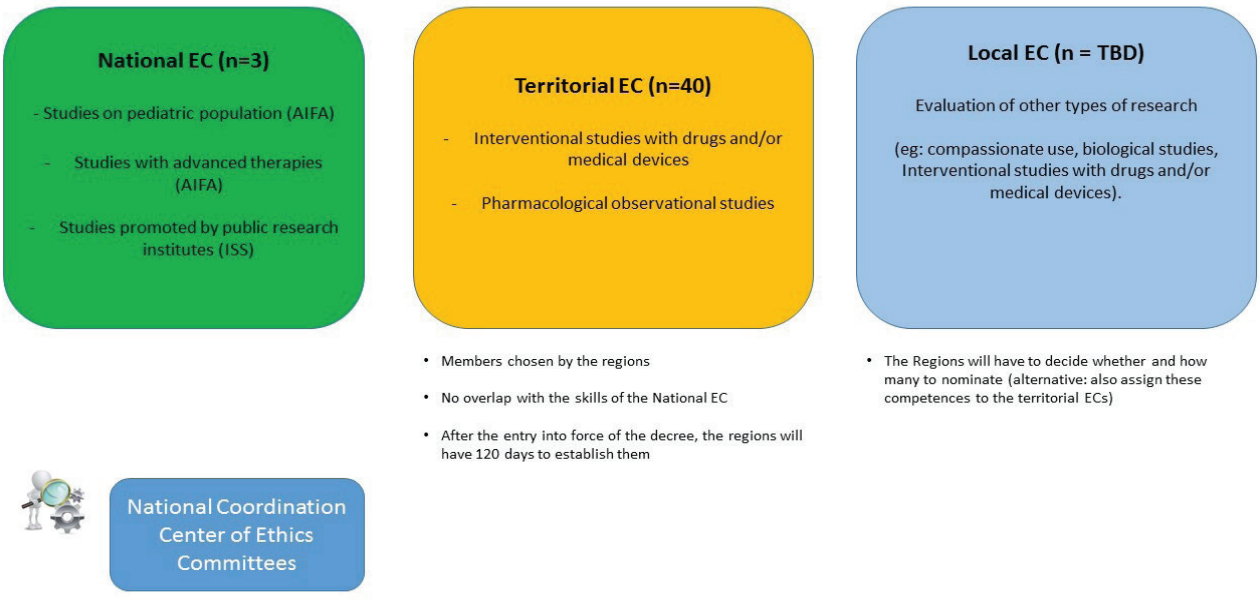

Figure 2. *Future organization of Italian Ethics Committees.*

The transition phase will also be delicate; any substantial amendments to studies still in progress according to Directive 2001/20/EC will be able to benefit from a single national opinion that will be expressed by the old coordinator EC or from one of the newborn territorial EC depending on the progress of reorganization (11).

Big questions also remain about the financial sustainability of the system. Despite the evaluation fees, standard at national level for interventional drug trials are increased compared to the past, the evaluation of a single committee for each trial it will certainly not guarantee a constant and heterogeneous incoming flow throughout the territory. Problems even greater for the regions that will decide to also maintain local EC, that probably will almost exclusively evaluate non-profit studies, therefore without evaluation fees.

The swift and successful completion of the reorganization will depend on three key factors: the adaptability of existing ethics committees; the competence of the regions in correctly managing the transition phase and the appointments of the components; the authority of the national coordination center of the ethics committees in carrying out its monitoring and control functions towards the territorial ethics committees.

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