each protocol has to be authorized ex-ante by a competent IRB. However, these directives have been integrated by each European country into national law with different features regarding the governance of these IRB systems. For instance, there are countries that have decided to adopt centralized systems (e.g. Croatia and its single national IRB), regional systems (e.g. France and its departmental system) or local systems (e.g. Italy and its local network of IRBs). Another issue concerns the requirement of a single opinion, rather than two. The European Directive suggests that pharmaceutical companies' experimental protocols can be evaluated with a single opinion by a competent national IRB. Afterwards, that single opinion can be extended to all the country's medical centers.[3] Also in this case there are national differences in the adoption of the Directive. Indeed, some countries (e.g. Italy) have decided to accept the single opinion but with a procedure of accepting/refusing that opinion by all competent IRBs involved in the authorization process (i.e. second opinion). Anyway, how do national choices in adopting the European Directives affect transaction costs? Coase's theorem suggests that the law can encourage bargaining by lowering transaction costs (Coase, 1960). According to his idea of market, this should be exactly the final target of this process in order to increase the pharmaceutical companies' investments in the testing phase (i.e. the exchange among companies and patients).

The two examples mentioned above will be relevant for the proposed analysis, since it focuses exactly on these key factors to estimate the relationship between clinical research and transaction costs, and to validate the idea of transaction costs applied to human experimentation.

In Italy, the European Directives on human experimentation have been acknowledged with the *Ministerial Decree of 06/11/2007* and *Legislative Decree no. 211 of 24/06/2003*. According to these laws, the Italian protection system includes a single opinion by the *coordinator* medical center and then a second opinion by each IRB competent for the *satellite* medical centers. This second opinion can accept, or not, the previous single opinion of the coordinator center. This is a specific feature of the Italian IRB system since, as mentioned above, the European Directive suggests that a single opinion should be valid for the whole country, without needing a second opinion by the satellite centers. Moreover, within the Italian governance, each region is entrusted with organizing and setting up a local network of IRBs (i.e. 21 competent authorities). This creates a system of 21 regional networks of IRBs with common features, as well as differences like, for instance, the administrative procedures to obtain the ethical opinions. Obviously, the exchange between the pharmaceutical industry and patients could be affected negatively only by the combination of these two features (i.e. local system and second opinion).[4] The awareness about the Italian difficulties on the European market of human

[3] In case of a negative single opinion, the trial cannot be proposed in that country again. Alternatively, the Directive suggests the possibility of obtaining an opinion from each territorially competent IRB.

[4] The average time the coordinator of an Italian Institutional Review Board takes to come to a decision is 35 days, while the satellite takes 50 days. Considering also that the authorization from the institution where the trial is conducted takes time, this means that it usually takes at least 4 months before an exchange can be performed. See AIFA, *La sperimentazione clinica dei medicinali in Italia, 8° Rapporto Nazionale, 2009.*