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# Clinical trials in nanotechnologies: The role of the research ethics committees (RECs)

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## ABSTRACT

Research Ethics Committees (RECs) can be defined as independent bodies composed of people with various fields of expertise, including medical and scientific but not only those, who are responsible for ensuring that the biomedical research projects involving human subjects conform to the principles of biomedical research. The RECs are an ethical guarantee to protect the safety, integrity and rights involved in the experimentations and to avoid the recurrence of scientific and economic abuse. They are also a legal guarantee because their reviewing activities are acknowledged in national and international rules and regulations.

Clinical trials in Nanotechnology may represent a challenge for RECs in so far they must verify that the chosen methodologies are the most adequate to the aims of the protocols, in a context, that of nanotechnologies, characterized by many unknown and uncertainties with regards to particle toxicity, and interaction with the human body.

For this reason, the REC should verify the risk to be assessed in terms of probability, magnitude and duration and verify the identification in the protocol of all those elements that may influence the risk, a risk that within nanotechnology represent an element hard to be identified. The role of RECs within Nanotechnology's clinical trials may be, then, decisive in the formulation of more specific operating procedures in this field.


## KEYWORDS

Nanotechnology (NT);
Nanomedicine;
Clinical trials;
Research ethics committees (RECs).

## RESEARCH ETHICS COMMITTEES (RECS): A BRIEF OVERVIEW

Research Ethics Committees (RECs) are independent bodies composed of people with various fields of expertise, including medical and scientific but not only those,who are responsible for ensuring that the biomedical research projects involving human subjects conform to the principles of biomedical research[1].

The biomedical research has always been carried out in a more less controlled way, and in accordance with the requirements of experimental methods. None the less, the specific concern regarding the ethical aspects involved in performing research became tangible

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just after the Second World War: the Nuremberg Code (1947), referring to the "absolute essentiality" of informed consent from the subject undergoing experimentation and the "objective" protection by the scientists, is one of the first bioethics documents ante litteram.

From that moment, the regulations developed along two lines: the doctrine of "human rights", culminated in the Universal Declaration of Human Rights (1948), and the specific guidelines for experimentation issued by international organisations (e.g. World Medical Assembly), which elaborated the Helsinki Declaration (1964 and revisions).

The Nuremberg Code and the first version of the Helsinki Declaration made the researcher responsible for the protection of the health and rights of the subjects involved in the experimentation, without mentioning the review commission, a role that, on the contrary, today has been recognised and envisaged by all the international guidelines on this field.

The review activities of the RECs is extremely important to the aim of protecting the life and the dignity of subjects involved in the research. The central part of the RECs activity consist in the examination of the experimentation protocol, the analysis and discussion of all its aspects. It is to evaluate not only the scientific validity but also the adequate protection of the experimental subjects.

For these reasons, the RECs are called to protect all the subjects involved in the experimentation in their safety, integrity and rights.

## ETHICS PRINCIPLE AND CLINICAL TRIALS

Several guiding principle to conduct research involving human subjects have been drown. As recalled by Sheremeta[2], these principles, expression of common values, may be summarize as follow:

- Respect for free and informed consent
- Respect for vulnerable persons
- Respect for privacy and confidentiality
- Respect for justice and inclusiveness
- Balancing harms and benefits
- Minimizing harm
- Maximizing benefit

Their core value is to promote and respect human dignity.

Nanotechnologies will faster clinical trials: fastening drug discovery and also as far as it regards genetic testing, fastening the methods to achieve sequences thanks to smart nanodevices. It is this the context where specific ethical concerns emerge; new genetic testing methods, in fact, "magnify a number of ethical challenge previously identified in the context of human genetics"[2]. So far, in the light of the mentioned principles in conducting clinical trials, according to this Author, some issues emerge. They concern both the informed consent and the autonomy of the subject of the trial. As regards the informed consent, the question concerns the possibility for human subjects to consent generally to future research involving their biological samples or genetic data derived from these samples. This will increase those issues already present in Biobanks. The autonomy will be concerned in so much new genetic testing methods will favour population genetic research, shaping a new balance between the autonomy of the subjects, in the way this is expressed within individualistic research, and communitarian norms supporting public health research.

## CLINICAL TRIAL IN NANOTECHNOLOGY: A "NEW" ROLE FOR RECS

The ethical evaluation of any experimental protocol involves providing an opinion regarding the rights of the subjects in terms of their physical, psychological and moral integrity, the principle of fairness and equal opportunities, the rights of the people who have access to the institute for assistance and who, may suffer the consequences and of the right of the physician taking part to carry out his main duty as a therapist.

Nanotechnologies, thanks to their properties, represent a challenge both for the scientific progress and for the Research Ethics Committees, as well as for the bioethical reflection[3,4].

With regards to the scientific progress it is expected the creation and use of structures, devices and systems with novel properties and functions because of their size, elements that are not met in material of higher dimensions. This will make possible the therapy of brain disease thank to the higher resistance, biocompatibility and integration of implants in the tissue[5], tissue regeneration[6], improved genetic testing capabilities, improved

surgical tools and more other marvellous applications.

With regards to the RECs, nanotechnologies represent a challenge insofar the novelty of these technologies and their usefulness in clinical research must safeguard the life and the integrity of the subjects of the research. As regards to both the discovery of new drugs and their delivery, the manufacture of novel biosensors based on magnetic nanoparticles will be used for the identification and validation of toxicity and cellular metabolism. It will be possible, therefore, to quicken the time of drug discovering. To this extent, it could be said that these are not concerns unique to nanotechnologies, but on the contrary they are likely to arise with many other technologies and applications undergoing the REC's opinion. However, the novelties of these technologies, given their cross-disciplinary nature and the properties of engineered nanomaterials, that differ substantially from conventional materials and technologies, make difficult the assessment of their risk[7-9], to the point that what might be non toxic in animal, with a low concentration exposure, it could be in human[10]. The new properties, exhibited by material nano engineered, will expand the risks and they will make this risks to be dissimilar to that one explored within other technologies.

The issue of introducing nanotechnology into clinical trials has been faced also at the within European level. In this light, the European Group on Ethics in Science and New Technologies (EGE) underlines the needs to distinguish questions according to: 1) their employment in the short, medium and long term; 2) to the specific use of the application (medical and non medical applications); and finally 3) the concept of health and disease. In particular, according to the EGE some questions should be clearly evaluated before introducing these technologies into praxis. These regard the respects of the dignity of people participating in nanomedicine research trials; the protection of the fundamental rights of people that may be exposed to free particles in the environment; the promotion of a responsible use of nanomedicine protecting both human health and the environment; and the consideration of some specific ethics issues (such as justice, solidarity, and autonomy) within nanotechnology's scientific domain[11].

With specific regards to clinical practice, the EGE identifies in the confidentiality of patient data and data protection some ticklish issues because many actors (specialists) may use these data[11].

Therefore, meeting the requirements of international guidelines may be difficult. Furthermore, according to the EGE, the uncertainties related to these technologies, their risks and the complexity which is part of them do not facilitate a realistic information; this means that the requirement to have an understood consent will also be difficult to be met.

In the light of evaluating the reasonableness of the foreseen risks in relation to the expected benefits for the subject or society, minimizing as possible those risks, the REC has the ethical responsibility to verify both the scientific merit of the study and the ethical justifiability and the validity of the information held in the information schedule nor the completeness of the information itself and in the acquirement of the informed consent[12].

The ethical and scientific evaluation of an experimental protocol means a judgment with reference to the respect of human life and physical, psychical and moral integrity. As regards the scientific merit, and with regard to nanotechnologies employment, it is to verify the suitability of the protocol in relation to the objectives of the study, the potential of reaching relevant conclusions with the smallest exposure of subjects, and the justification of predictable risks and inconveniences weighted against the anticipated benefits, keeping in mind that many toxicological studies on nanoproducts are still undergoing (including the permanence in the blood stream and vital organs of nanoparticles). The ethical justification is more involved in searching for an informed consent with an adequate information for the subject, an information that must consider the many unknowns related to nanoproducts, such as toxicity, and toxicity evaluation and management.

Much more in this novel field than any other, the REC must verify that the chosen methodologies, involving the use of nanotechnologies as technologies or in their smallest elements (nanoparticles), are the most adequate to the aims of the protocols. In doing this, the REC should verify the risk to be assessed in terms of probability, magnitude and duration and verify the identification in the protocol of all those elements that may influence such risk. In doing this, RECs should taking into account the fact that the traditional methods of evaluating toxicity are not suitable for nanotechnologies.

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This require a deeper examination of the study. Furthermore, the Committee has to make sure that any identified risk be associated to measures to prevent, minimize and monitor such risk as much as possible: the determination of the levels of risk and the associated potential benefits will guarantee the protection of the subjects. The decision involves, than, the responsibility of the technical and scientific opinion of experts.

As it regards the risk/benefit analysis, in the attempt to limit or avoid the risk, and especially in the criteria for the suspension or interruption of the participation of the subjects, in all the aspects in which a specialist, technical competence is necessary, the opinion of "technical" members will be extremely important. The expert in nanotechnology will "guide" the non expert members in reaching those information and elements that are relevant to make an opinion. The members with non medical and scientific expertise will be called to pay a particular attention to the ethical, legal and also psychological aspects, because of the impact that the experimentation may have on the subjects taking part (for example evaluating whether the participation in the experimentation will excessively condition already difficult or precarious situation caused by the pathology) but also on the community concerned.

Clinical trials are an important mean to discover new drugs and improve tools for preventions, diagnosis and treatment, and when ethically conducted they represent a good for the person underling also the importance of the science.

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