



Presidenza del Consiglio dei Ministri

NATIONAL BIOETHICS COMMITTEE

BIOETHICAL PROBLEMS IN CLINICAL TRIALS WITH NON-INFERIORITY DESIGN

(24th of april 2009)

abstract

The opinion examines the clinical trials on drugs which do not present an “added value” in terms of greater efficacy or lower toxicity with respect to drugs already existing in commerce. These are trials which, unlike the “superiority” or “equivalence” designs, present some bioethically important issues.

Starting with a definition of “non-inferiority” as “similarity within predefined limits”, the document critically examines the scientific reasons adopted as a justification for such studies (the possibility to offer patients a useful alternative, better tolerability, price reduction), stressing (also by means of examples) how only “superiority” testing has an adequate motivation in the interest of the patient, while the “noninferiority” testing mainly answers the needs of the pharmaceutical industry (less risk, lower costs).

The NBC highlights the inadequacy of the justification of “non-inferiority” at the scientific and ethical level, referring to the reduced scientific validity of the research, the methodological-clinical interest and the definitive guarantee of effectiveness (guaranteed instead by drugs that have already been experimented and are readily available), the potential “conflict of loyalty” on the part of the doctor whose first duty is to offer the patient a suitable therapy of substantiated efficacy (not guaranteed by the drugs proposed in the trial with respect to standard treatment), the lack of transparency concerning the informed consensus by the subject who undergoes the trial and who is not given sufficient information about the nature of the trial that is to be carried out.

The NBC’s opinion reconfirms the principle, dealt with in numerous international documents, according to which the specific interest of the patient must not be subordinate to other interests including commercial and advertising ones. In particular the NBC recommends that “non-inferiority” trials are presented with greater transparency and that the ethical committees carefully examine the methodology with which they are designed, approving only the “superiority” testing, which can bring huge advantages to the people participating in the trial or to patients who will use the drug in the future.