



Presidenza del Consiglio dei Ministri
NATIONAL BIOETHICS COMMITTEE

**CONFLICTS OF INTERESTS IN BIOMEDICAL
RESEARCH AND IN CLINICAL PRACTICE**

8th of June 2006

CONTENTS

Presentation	3
Introduction	4
The problem of the “false facts” in science	5
Scientific “false facts” and methodological distortions	5
Ethics of research and conduct in clinical medicine	7
Contemporary clinical research and industry	8
The conflict of interest of the doctor researcher and the clinician	9
The possible remedies	10
Bibliography	15

PRESENTATION

Upon proposal of prof. Giovanni Federspil, in the plenary meeting of the 24th of June 2005 the National Bioethics Committee unanimously decided to set up a working group on the subject of the conflict of interests in medicine. Various members of the NBC joined the group including Profs. Salvatore Amato, Mauro Barni, Luisella Battaglia, Paola Binetti, Adriano Bompiani, Luisa Borgia, Cinzia Caporale, Lorenzo d'Avack, Maria Luisa Di Pietro, Luciano Eusebi, Angelo Fiori, Carlo Flamigni, Laura Guidoni, Aldo Isidori, Demetrio Neri, Pasqualino Santori, Giancarlo Umani Umani Ronchi. Prof. Federspil was unanimously appointed coordinator of the group. After a year of work with numerous meetings of the group, Prof. Federspil delivered the draft of the Document agreed upon by the group to the NBC. The Committee, greatly appreciative of the work carried out by Prof. Federspil and the results achieved, expressed its unanimous approval in the plenary meeting of the 8th of June 2006, with a slight but appropriate change in the title.

The delicate nature of the subject dealt with in this Document hardly needs to be stressed. The crisis of Hippocratic medicine, the spread of a reductively contractualist vision of the doctor/patient relationship, the influence that utilitarian models of thought (often not well understood and above all badly applied) has on most contemporary public opinion, the exasperated technisation characterising the most recent and most efficient diagnostic and therapeutic methodologies cannot but exasperate issues that were well-known to traditional medical ethics, but which have now become such as to require new rigid forms of approach. One must not be eluded that bioethics alone can adequately deal with problems of such dimension, without further forms of biojuridical and above all biopolitical support. It can however – and therefore must – take on the task of judging and reporting the new forms of alteration in the professionalism of the researcher and medical practice, which have specific ethical repercussions. By publishing this Document, the NBC is certain that it has opened up the road to reflection and commitment in this field which will be exemplary, at least in the short and medium term.

*President of the National Bioethics Committee
Prof. Francesco D'Agostino*

INTRODUCTION

Medicine is a complex polymorphous science, having relations of different types, with society and the institutions produced by it. These relations involve both biomedical research and clinical medicine, that is to say, the applied medicine practised daily in surgeries, x-ray departments, laboratories and in hospital wards and teaching hospitals.

Modern biomedical research can be carried out, overall, only with the use of huge capital. While it is in fact true that some research can be done with the use of relatively inexpensive equipment and materials, it is just as true that many other types of research – especially of an applicative nature – need extremely sophisticated instruments and a complex structured organisation which often goes beyond the boundaries of single states and has to be kept operational for years, with great expenditure of human and economic resources.

Similarly, clinical medicine is today practised with the use of elaborate equipment and investigation techniques and treatment of patients which weighs heavily upon social expenditure. In order to have a real idea of the economic resources that are taken up by medicine, it suffices to think of the huge radiological equipment, the computerised axial tomography, the nuclear magnetic resonance, modern microscope techniques, transplant surgery and the widespread use of costly drugs.

It is therefore easy to understand how the use or non-use of a technique, a piece of equipment or a drug can move considerable sums of money in one direction or another.

This situation, which is strictly linked to the quantity and quality of the investigations and therapies available to citizens today, is the origin of an evident bioethical problem. The doctors who deal with applied research and the actual problems of the patients are obviously social subjects, who work in the human community and who therefore have desires, plans and ambitions like all the other members of such a community. Hence, working in a world where the economic interests coming into play are often huge, they are greatly exposed to possible conflicts of interest.

Over recent years this argument has been the subject of numerous articles in international scientific journals and, in some of its aspects, of normative measures aimed at guaranteeing the correct carrying out of research and experimentation activities¹.

Very recently a number of scientific organisations have dealt with the issue and have introduced some practical norms in an attempt to make the possible conflicts of interest of the various researchers explicit².

Despite the attention paid to the conflict of interest in the world of medical research, the problem has not yet been analysed in any depth or satisfactorily by the bioethical world. Without claiming to deal with all the aspects of such a complex subject, it seems opportune to dedicate a number of

¹ With regard to this see *Jama* 2000, 284, pp. 2234 - 37; *Jama* 2003, 290, pp. 2521 – 22; *Jama* 1998, 279, p.1067; *Lancet* 1997, 348, p. 627; *Lancet* 1997, 349, pp. 327 – 31; *Br Med J* 1994, 308, pp. 4 – 5; *N Engl J Med* 1989, 321, pp. 86 – 92; *N Engl J Med* 1997, 336, pp. 1666 – 67; *N Engl J Med* 1989, 321, pp. 464 – 66; *Nature* 1992, 360, p. 205.

² As for example, the SIMI made a declaration obligatory for its members concerning the possible personal interests of a speaker in the field of research in which he is publishing a piece of work or giving a paper at a conference.

reflections to the question of the conflict of interest, which might be the starting point for further in-depth studies.

The phenomenology of the possible conflicts of interest is vast and highly polymorphous, the very concept of 'conflict of interest' not always being clear and univocal. According to one widely accepted definition, 'there is a conflict of interest when one finds oneself in a condition in which the professional judgement concerning a primary interest (the health of a patient or the truthfulness of the results of research or the objectivity of giving information) tends to be unduly influenced by a secondary interest (economic gain, personal advantage)' (Bobbio 2001).

The problem of the 'false facts' in science

Modern science is presented as objective knowledge, which sets out to describe and explain natural reality just as it is. This aim was repeatedly challenged during the XX Century and contemporary epistemology has demonstrated how scientific knowledge is partial knowledge, approximate and always open to being corrected – that is, reformable – rather than incontrovertibly true knowledge. In other words, an absolute realism of science is presented more as a regulatory ideal than as a definitive achievement.

Despite these intrinsic limits, there is no doubt that modern scientific knowledge is presented as objective, reliable and rationally founded knowledge. These general characteristics of naturalistic knowledge are founded on the objectivity and truthfulness of factual records that are carried out by scientists. Even if scientific assertions cannot aspire to absolute completeness and neutrality, there can be no doubt that the scientific code of ethics establishes, as a fundamental and minimal duty of the researcher, the obligation to make one's own observations in such a way that they are as faithful and complete as possible.

Despite these ethical imperatives, the history of science bears witness to how in the last Century numerous conspicuous false facts were claimed³.

In reality, the phenomenon of 'false' scientific facts is not easy to interpret. While in many cases there can be no doubt with regard to the will of the researcher to deceive the scientific community, in others the boundaries between the authentic 'false fact' and imprecision or the poor methodological rigour of the research certainly appear more unclear.

Scientific 'false facts' and methodological distortions in medicine

In a discipline like medicine, in which the subject being studied – healthy and ill people – is extremely complex and very often observations lack the precision and objectivity that are more easily obtained in the sciences of the inorganic world and in the other branches of biology dealing with organisms that are more simple than the human one. Furthermore, the points of view from which a specific biomedical problem can be looked into are very often so

³ It suffices to mention the cases of William T. Summerlin, John Darsee, Soman and Felig, John Long (Kohn, 1991) to have the proof that researchers do not always observe the rules that should constitute the ethical basis of their profession.

numerous in medicine that it is not easy to establish what the best approach is in the different circumstances.

It therefore appears evident how in biomedical research – and particularly in research more closely connected to clinical problems – the approaches of a researcher can be directed and motivated not only by cognitive problems or by the exclusive desire to find a remedy to morbid problems, but also by personal problems or by those linked to the institutions where the researcher works.

This complex situation in which biomedical researchers often find themselves, and above all those working with therapeutic problems, has aroused the suspicion that a more or less relevant amount of the research carried out today is not as neutral and objective as it should be⁴.

In a parallel way, medical practice can also be easily influenced by the world of industry which operates in close contact with doctors practising in healthcare structures⁵.

There is no doubt that today the industrial world finances a very considerable part of clinical research in one way or another. According to some assessments, about ¾ of biomedical research currently carried out in hospitals and clinics (and in a lesser way also in non-clinical research), is backed by industry. Of course, the contribution by industry is not limited to financing the research that comes into the production interests of the companies, but is extended to supporting studies of purely theoretical interest that are conceived and carried out as a result of the interest and initiative of researchers belonging to public facilities.

In a Document published on the 22nd of March 2005, an ad hoc committee set up by the House of Commons of the UK Parliament declared that: "the influence of industry has spread to such an extent that now numerous activities move against public interest....".

In Italy, as in other countries, single scholars have maintained that research and clinical practice are considerably influenced by industry and that clinicians are exposed to the danger of taking decisions that are not always linked to the patient whose interest they have the duty to take care of.

Even though a prejudicial attitude is manifest in many of the reports made, hostile to the world of industry where every intervention is seen as a potential danger for the neutrality of research and good clinical practice, there is no doubt at all that the situation that has come to be raises serious bioethical issues to which it is indispensable to try and give an answer and for which general rules of conduct must be outlined.

⁴ With regard to this, see the international and Italian regulations on clinical experiments. The principle references of the Italian regulations for the trials relative to drugs can be found on the site of the Agenzia italiana del Farmaco (AIFA). Among these is highlighted the Ministerial Decree of 15.07. 1997 which sets down a series of indications on instruments of protection (known as Good Clinical Practices) and which set up the Ethics Committees for clinical trials, and the following M.D. of 18.03.1998 – Reference guidelines for the setting up and functioning of the ethics committees. See furthermore Legislative Decree No. 211 of 24.06.2003 – Implementation of the directive 2001/20/EC relative to the application of Good Clinical Practices in the carrying out of clinical drug trials for clinical use, which foresees a series of applicative decrees.

⁵ In confirmation of all this, a recent survey in the US carried out by the Health Partners Research Foundation of Minneapolis, conducted on 3,247 researchers, highlighted how a considerable number of those interviewed admitted having put forward incorrect interpretations of the data obtained and how about 15% confessed to having modified their own study upon pressure from the commercial sponsors (Corriere della Sera 14-6-2005).

Ethics of research and conduct in clinical medicine

Since medicine is made up of two parts, distinct but closely connected – research and clinical activity – it is opportune to keep the treatment of the first separate from the second here too.

Biomedical research is made up of two parts – the research that is carried out on parts of living organisms or on laboratory animals or on healthy or sick subjects with the aim of describing or explaining normal and pathological biological phenomena, and the research that is carried out on ill human subjects, with the aim of deciding on diagnostic and/or therapeutic treatment that will improve the course of the illness and the prognosis of morbid processes affecting the patients. The first constitutes the sector of medicine which is generally called experimental medicine, while the second is called *clinical research*.

The question of the conflict of interests arises in most cases in clinical research since it is in this sector that considerable economic resources and sophisticated analytical instruments are usually used.

The general ethics of research requires the application of clear standardised rules: researchers must refer the results of their observations and experiments in full, scrupulously and faithfully, without eliminating the data that do not agree with their initial hypothesis. They must fully describe the techniques used to carry out their research and the type of data analysis used to highlight the phenomena that appear to be most significant. If the slightest doubt exists that something did not work as it should have done during the experiment, the scientific observations must be repeated until the results obtained have become constant and superimposable. The results and techniques of their studies must not be kept hidden and, when published, no parts of the results must be left out, thereby favouring some conclusions rather than others. Lastly, they must not be influenced by personal interests of any kind whatsoever: economic, social, personal prestige, etc. The basic mental approach of researchers must be inspired by a fundamental humbleness before nature and its laws; they must recognise, in fact, that they are simple disciples asking questions in order to learn and can never think that they can superimpose their own ideas onto nature. A sociologist has summed up the values that must inspire the ethos of the researcher in an acronym – Cudos – which unites Communitarism, Universalism, Disinterest and Scepticism as methodological approach.

These general rules are sufficient for an honest practice of studies in many naturalistic disciplines. They are, for example, adequate and sufficient for a botanist as they are for an astronomer or a palaeontologist. For biomedical sciences, on the other hand, the ethical problem immediately becomes more complex since experimental medicine already poses the morally relevant problem of the use of laboratory animals to acquire greater knowledge of the living world. It is in fact evident how a lot of research carried out by biochemists, physiologists, embryologists, pathologists, etc. has no immediate consequence of a practical nature and is only carried out with the aim of checking a specific biological hypothesis.

In clinical research the issue becomes more complex and difficult since the researcher, in carrying out his own studies intervenes and works on other men and can more easily modify their organism and lifestyle or, even their fate.

In reality, a more detailed investigation can show how the conception of an ethics of science that identifies with an ethics of knowledge and neutral impartial truth (Gismondi 1997), is today clearly insufficient to deal with the many issues raised by modern research.

With regard to medicine, the ethical problem of human experimentation has already been dealt with by this committee (The experimentation of drugs.17th of November 1992), nevertheless this problem goes beyond the solutions already discussed and takes other issues into consideration.

With respect to the problem already dealt with, which concerned above all the rules and procedures of clinical trials, informed consent, the protection of patients, pharmacovigilance, etc., the present one can appear to be totally banal since it seems obvious to say that the behaviour of a researcher should not be influenced by external factors for the intrinsic ends of science. Nonetheless, the question will not appear to be so foregone if one considers that the problem being debated is presented as *a problem of ethical limitations* rather than of ethical principles. From this point of view it is no different from other bioethical issues – for example, from the question of persistent therapy – in which it is easy to accept the basic principle, but it is extremely difficult to identify the limits within which that principle is valid and must be applied.

Contemporary clinical research and industry

Today the world of clinical research is closely connected with the social production reality constituted by industry and the presence of the institutions, represented by universities and healthcare facilities.

When a result of basic research (explicative hypothesis, technological instrument, diagnostic procedure, drug or clinical trial) leaves the closed environment of the laboratories and goes on to be used, it comes into contact with a much bigger environment than the one where it was born and had lived, and finds itself exposed to very strong pressures of different types.

A drug for example is evaluated for its therapeutic possibilities that it may have in the various social contexts of the same country and in different countries of the world. At the same time, it is also evaluated for the several other factors: the possible side effects, the cost of transforming it from a potentially effective molecule with therapeutic effects into a marketable drug, the possible return and profits that it can make, the similar drugs with which it will have to compete, the foreseeable length of its presence on the market, and the reception it will receive in the medical world, etc.

As the pharmaceutical companies have to make a profit in order to stay in the market, they need to try to promote the sale of their own drugs (or, for companies not producing drugs, the sale of their own products: diagnostic kits, surgical devices, diagnostic equipment like scans, stents, bone density measurers, etc.). If one considers that the average cost of putting a drug onto the market amounts to hundreds of million euros, it is easy to understand what the entity of the product must be to be able to amortise the expenses sustained.

Before the industries come the doctors, who inevitably become the terminals of pressure made by the industries to realise their own economic ends.

Between the industries and the healthcare world are the public institutions, which take various measures to contain drug spending, adopting different measures: regulation of drug prices, stratification of drugs into different categories, specific packaging of products containing the pharmacological principle, but without brand name at a lower price, prescription control, exclusion of ineffective products or ones that have been substituted by other more effective ones, etc.

The strategies used by industry to lead doctors to prefer their products are several and differ from each other. Some of these appear to be completely licit, while others, which will be looked at more in detail in the conclusion of this document, are clearly debatable from an ethical point of view.

The conflict of interest of the doctor researcher and the clinician

In Italian society today, as in all the other countries of the Western world, the pharmaceutical industry and the other companies producing materials and instruments for the healthcare service, powerfully interact with such system. It is certainly no mystery that a considerable amount of applied medical research is carried out upon initiative or even upon commission of the industries that are very keen on the success of new drugs or new technological products. In this way a relationship is created of the 'researcher/client' type between the doctor carrying out the research and the industry that conceives, plans, organises, finances and lastly, edits the publication of the research itself.

It appears evident that in some cases the doctor-researcher figure can become subaltern to that of the client: in fact, while an interest of the industry consists in valorising the product in which it has invested its resources to the maximum, the aim of the doctor-researcher should be that of describing how things are without being influenced by different ends. It is just as clear, furthermore, that even a researcher with no contacts with industry has a personal interest in concluding his research positively: in fact, studies demonstrating the effectiveness of a drug or the clinical usefulness of an instrument are usually more appreciated and more rapidly promote the career of a researcher than studies giving a negative result. However, in the case of a sponsored trial, the interest of the financier is added to the personal interest of the researcher, thus creating conditions that facilitate the creation of a conflict of interest.

Conflicts of interest can be of two different types: direct and indirect. The first type takes place when the doctor-researcher receives direct payment for his work from the industry. The indirect conflicts are when the doctor-researcher doing the research involving a product of an industry, receives various forms of fringe-benefits from this industry (for example, free participation at congresses, trips, grants for himself or for his collaborators, giving of scientific equipment 'on gratuitous loan', etc).

It is easier for these conflicts of interest to take place in those fields of pathology in which morbid alterations are particularly widespread, the pathogenetic mechanisms very long or even indefinite. Examples of these 'at risk of conflicts' spheres of study are the antihypertensive, hypolipidemising or anti-osteoporosis therapies.

It is inevitable that the medical world is sensitive to the economic backing that industry offers research and/or professional refresher courses. A doctor's

gratefulness clearly conceals a considerable danger for the intellectual independence of the clinician. The choice and prescribing of medicines (like diagnostic tests or instruments or equipment) can be widely influenced by the doctor's state of mind, which could be led into preferring one drug instead of another, not because of the pharmacological or therapeutic features of the molecule, but owing to the relations that he has with a certain industry.

This situation, with dangers on all fronts, has been compared to the porcupine dance, or rather to a situation in which the two sides are obliged to dance together without however getting too close for fear of hurting one another.

The possible remedies

The American scientific world has become aware of the situation that has come to be in the last decade and in 1990 the American Medical Association included the Opinion expressed by its Ethical and Legal Commission into its Code of Ethics for the medical profession. In Italy only two medical-scientific associations have dealt with the problem of the conflicts of interest until now⁶.

In 1999 FNOMCeO included an Article (Art. 73) on conflicts of interest in its Deontological Code. This article however concerns the conflict that can arise between the clinical activity of a doctor employed in the healthcare service and free-lance clinical activity.

Different approaches can be used when dealing with this phenomenon. On the one hand, there is the standpoint defended by the British Medical Journal⁷, according to which the conflict of interests would in itself be morally reprehensible and it is therefore to be hoped that a separation of the medical world from the industrial one may be achieved. On the other hand there is the standpoint described in the work of a number of sociologists⁸, according to whom it would be opportune to overcome the definition of 'conflict of interests'. The conflicts going under the name of 'conflicts of interest' are not real conflicts, but 'social interactions with a strong speculative nature'. The social relations as such would not be dishonest but only the behaviour of the single persons: pharmaceutical representatives, publicists, doctors prescribing medicines, etc.

⁶ These societies are the Associazione Nazionale Medici Cardiologi Ospedalieri and the Società Italiana di Medicina Interna. At its 102nd National Congress (2001) the latter held a Round Table entitled "The neutrality of science. Conflicts of interest" and resolved that in the papers presented at their congresses and in those published on their official journal (*Annali Italiani di Medicina Interna*) the authors must declare the presence or absence of conflicts of interest *. In reality, such a declaration, praiseworthy as it may be, does not seem to constitute an adequate instrument to check such a widespread phenomenon as the conflict of interest is today. **The compulsory declaration is the following: "The author denies having any connections of an economic or professional nature with industries or organisations, as a result of which a conflict of interests may arise concerning the matter discussed in this presentation"*.

⁷ See R. Smith, *Medical journals and pharmaceutical companies: uneasy bedfellows*, in "Br Med J", 2003, 326, pp. 1202-05. R. Smith, *Conflict of interest and the BMJ*, in "Br Med J", 1994, 308, pp. 4-5. R. Smith, I. Roberts, *An amnesty for unpubliushed trials, send us details on any unreported trial*, in "Br Med J", 1997, 313, p. 622.

⁸ See Ivan Cavicchi, *Il medico tra due conflitti: l'economia che determina e la società determinante*, in "Ann Ital Med", Int 17 (Suppl 1), 2002, pp. 143S-149S. Ivan Cavicchi, *Implicazioni della neutralità tra scienza ed economia*, in "Ital Med", Int 18 (Suppl 1), 2003, pp. 203S-206S.

What all these subjects have in common would be the deliberate diffusion of false information or the distortion of facts leading to conduct for the purpose of guaranteeing personal gain. The conflict of interest would therefore be a form of agiotage that would come under the sanctions foreseen by the Penal Code (Art. 501) and the Civil Code (Art. 2628), and the 'physical evidence' would be the dishonest information.

Both positions appear extreme and lead to undesirable consequences: the first would greatly harm applied biomedical research as a whole, and would slow down any therapeutic progress; the second would hit only the conduct whereby wrong information is given. This obviously implies that it is possible to clearly distinguish true scientific statements from false ones and disregards the fact that scientific claims are usually characterised by more or less high degrees of credibility (Hempel, 1968).

Instead, as often declared by a number of sources, it must be recognised that the conflict of interests tends to arise as a condition that could give place to or even promote ethically reprehensible conduct. In other words, conflict of interests is not a conduct, but a 'condition' and, therefore cannot be reprehensible in itself: in fact, in every man's life he finds himself in conditions of conflict of interests on numerous occasions and this status cannot be eliminated from human life. Big advantages are to be obtained from an industry and an absolutely upright conduct can be equally maintained, just as one can have weak conduct before someone who can give us an insignificant gift. Nobody can deny however that the first condition is ethically much riskier than the second, and therefore it seems ethically important to recognise the limit beyond which a conflict of interests increases forms of ethically censurable conduct with great probability.

What bioethics can do is to set out a limit that makes reprehensible conduct difficult to practise or that establishes where a status of conflict generates reprehensible conduct. Of course, the idea of being able to fix this kind of limit in such a precise and definitive way appears rather naïve since the conflict of interests, for the very reason that it is a condition and not a conduct, becomes morally reprehensible only when it causes reprehensible conduct.

It is evident how the context of scientific research and clinical practice, intentionally not dealt with in this document, are closely connected by the methodological and ethical correctness with which scientific data are produced. A clinical trial and/or its corresponding publication, which contains partial data will heavily condition the correct use of a drug in clinical practice, since the prescription of a pharmacologically active substance is substantially founded on results published in scientific literature. A distinction must be made however between the conduct of a researcher facing a scientific problem posed by a drug, studying its effects on a sample of subjects and that of a clinician who finds himself treating a single person.

In the first case the general interests of the patients must be assessed above all and any conduct will be censurable which describes the advantages of a drug with respect to other similar drugs in a way that is basically false, or which conceals its drawbacks or dangers.

In the case of clinical activity, the solution to an extremely difficult problem like this one can only be found in the reference to a principle which, in all circumstances, is superior to the one caused by the conflict of interests. This principle can be no other than the welfare of the patient: every time that a conflict of interests produces clinical conduct in which the interest constituted

by the well being of the patient is put after a different interest, that conflict must be judged as being ethically censurable.

In other words, the ethically censurable conduct will first of all consist in a decision which, on the basis of his general knowledge or the experience that a single doctor has of a single patient, chooses a drug or opts for diagnostic treatment that is the least suitable for the individual pathology of that patient⁹.

In this case, the ethically censurable conduct does not derive from the breach of the general rules of research, but from not adequately considering the most reliable knowledge existing at a certain moment and by not giving the well being of the patient priority¹⁰. In fact, in clinical practice, only the doctor that is acquainted with the pathological condition of the single patient, his/her personality, existential situation and the desires expressed, can recognise what is good for that person.

Final considerations

Recently some of the situations that frequently arise have been described, in which the objectivity of research and that of the scientific information given to doctors can be jeopardised:

1) industry does not always give doctors information that is complete and neutral, but targeted information, created in its own offices;

2) the drugs produced are often duplicates of other already existing medicines (the so-called me-too drugs) which present no advantages with respect to the latter and which are sold at a higher price. The industry usually promotes the most recent and expensive drugs and for this purpose lavish various types of 'gifts' on the doctors leading to an attitude inclined to hyper-prescription by the same or to the prescription of the most expensive drugs;

3) industry controls and directs research by means of funding given to universities;

4) industry sometimes interrupts non-favourable research or hinders its publication. In other cases it distorts on-going research, substituting the primary end points with surrogate ends;

5) the rough data of clinical-pharmacological trials often remain in the hands of industry and are never put at the disposal of the researchers who produced them. They are given the data only when they have been reprocessed by the statistics offices of the companies;

6) being the 'owner of the results', the industry does not publish the negative ones;

7) scientific journals do not publish articles containing negative data since it is of little scientific or commercial interest;

8) the industry conditions, by means of publicity, the big medical journals, whose referees often have relations of economic dependence with the companies;

⁹ Of course insofar as in this opinion pharmacological therapy is dealt with in particular, similar considerations are true for all types of therapy and diagnostic procedures.

¹⁰ It is therefore hoped that the professional associations carry out controls on their members, assessing the clinical conduct of doctors and attempting to highlight those situations in which the conflicts of interest have generated ethically unacceptable clinical conduct.

9) the doctors who draft the reviews or guidelines are very often not truly independent of industry.

10) even the public administrations are often not independent of industry.

This incorrect conduct – which is moreover not extended to all industries – does not exclude the fact that a correctly interpreted and regulated free market regime has had and may have a central role in the progress of biomedical research and in the development of technologies relative to it. This conduct however can create conditions of conflict of interest on the part of biomedical researchers and doctors towards the companies with which they are in touch.

Given the complexity of the real situation, the possible remedies do not appear to be without difficulties and can certainly not lead to definitive solutions. The role of the ethics committees seems to be fundamental in this field, in checking experimental protocols put to their approval, evaluating any possible risks inherent in the research, in the light of the benefits which could in fact be obtained for the single patient and the whole community.

Moreover they could promote the diffusion of knowledge gained from clinical research, asking for commitment in the diffusion and/or publication of results by the experimenters, in the respect of the laws in force on the privacy of data and patent protection. In the case of clinical trials not sponsored by industry and carried out in accordance with the so-called ‘no profit’ decree (M. D. 17 .12. 2004: Prescriptions and conditions of a general nature, relative to the carrying out of clinical drug trials, with particular reference to those for the improvement of clinical practice, as an integral part of healthcare), the ethics committees also have the task of verifying that trials with commercial ends are not carried out in this capacity. In this case the ethics committees are explicitly called upon to verify that a declaration is signed on the conflict of interests, foreseen in detail in an attachment to the decree.

The ethics committees themselves can perform the task of ‘guarantors’ only if they are set up and organised in such a way as to ensure their independence from any form of hierarchical subordination by the structure in which they work. Even in the ethics committees the absence of any form of conflict of interests of the voters with respect to the research protocols proposed must be guaranteed.

As far as concerns the problems linked to research, the first measure should regard the transparency of the various situations. Each sponsorship and each link, be it direct or indirect, existing between industry and the single researcher or the institution in which he works, should be declared publicly and described without concealing anything in its real terms when the results of the research are made known or used to support therapeutic choices. The sponsoring industries should always give all the rough data obtained to all those who have taken part in a study. The interpretation of such data should be discussed together among the company representatives and the those of the various research groups that carried out the study. The final paper should be approved by all those who participated in the investigation and, in the case of contrasting interpretations, should include the different opinions.

Since the failure to publish the results of a non-favourable or little favourable trial to a specific treatment represents a factor that distorts the overall knowledge of the scientific community, the ethics committees should make every possible effort so that the outcome of all clinical research begun is published. This should be true also and above all for the studies that are interrupted owing to the obvious poor efficacy of the therapy being tested or

owing to the presence of considerable side-effects. In fact the absence of the publication of the negative effects of research in literature produces a very serious information gap, both in the experimental context (allowing useless duplications of similar research, with an unacceptable waste of economic resources which could be used for other sectors), and in the clinical context (not permitting the doctor to know all the information necessary so as to guarantee each patient the due combination of “best therapeutic result/least exposure to the risk of adverse events”).

It is important to point out that a piece of research, at a moral level, belongs to all those who, together, conceived and carried it out and who drew and demonstrated their conclusions, independently of their juridical position (employees of the public sector, private companies, individual professionals, etc) or professional one (biologists, chemists, doctors, statisticians, physicists etc.) in which they found themselves at the moment of carrying out their work. Therefore, it must be stressed how the role of researchers who work for the PA must in no way be less important than that of those who financed the research.

Lastly, the increased use of revealing the results of an experiment by means of mass media seems unethical, before the results have been published in scientific journals and thus submitted to the scrutiny and judgement of the scientific community. Such conduct can in fact lead public opinion to have false hopes or dangerous alarmism, even before the results have had the necessary confirmations or denials.

BIBLIOGRAPHY

AA. Vari, *Etica della conoscenza scientifica*, Istituto della Enciclopedia Italiana, Rome 1989.

AA. Vari, *Filosofia della scienza e problemi etici*, Borla, Rome 1993.

AA. Vari, *I conflitti d'interesse in medicina*, L'Arco di Giano No. 23, 2000.

AA. Vari, *Comprare e vendere in medicina*, Janus No. 17, 2005.

Agazzi E., *Il bene, il male e la scienza*, Rusconi, Milan 1992.

Bencivenga E., *I passi falsi della scienza*, Garzanti, Milan 2001.

Bobbio M., *La neutralità della scienza: la situazione italiana*, IN "Ann. Ital. Med. Int.", 2001,16 (Suppl. 1), pp. 2155-2185.

Bobbio M., *Giuro di esercitare la medicina in libertà e indipendenza*, Einaudi, Turin 2004.

Cavicchi I., *Il medico tra due conflitti: l'economia che determina e la società determinante*, in "Ann. Ital. Med. Int.", 17 (Suppl 1), 2002, 143S-149S.

Cavicchi I., *Implicazioni della neutralità tra scienza ed economia*, in "Ital. Med. Int.", 18 (Suppl 1), 2003, 203S – 206S.

Di Trocchio F., *Il genio incompreso. Uomini ed idee che la scienza non ha capito*, Mondadori, Milan 1997.

Federspil G., *La medicina tra arte e scienza: questioni di metodo*, in "La qualità in medicina tra etica ed economia. Riflessioni sulla professione del medico degli anni duemila", Atti del II Convegno Nazionale sulla VRQ, Publisher FNOMCeO, Firenze 1995.

Federspil G., *E' davvero possibile servire due padroni?*, Società Italiana di Medicina Generale (SIMG),1996, 10, pp. 5-11.

Freemantle N., Hill S., *Medicalisation, limits to medicine, or never enough money to go round*, in "BMJ", 2002, 324, pp.864-865.

Gismondi G., *Etica fondamentale della scienza*, Cittadella Editrice, Assisi 1997.

Hempel C.G., *Filosofia delle scienze naturali*, Il Mulino, Bologna 1968.

Jacobelli J. (a cura di), *Scienza ed etica. Quali limiti?*, Laterza, Rome-Bari 1990.

Kohn A., *Inganni ed errori nella scienza*, Zanichelli, Bologna 1991.

Moynihan R., Cassels A., *Farmaci che ammalano e case farmaceutiche che ci trasformano in pazienti*, Nuovi Mondi Media, San Lazzaro di Savena 2005.

Skrabanek P., McCormick J., *Follie e inganni nella medicina*, Marsilio Editore, Venice 1992.

Vineis P., Capri S., *La salute non è una merce. Efficacia della medicina e politiche sanitarie*, Bollati Boringhieri, Turin 1994.

D.M. 15 luglio 1997, Recepimento delle linee guida dell'U.E. di Buona Pratica Clinica per l'esecuzione delle sperimentazioni cliniche dei medicinali, Off.Gazz. No. 191 of 18 August 1997, Suppl Ordinario No. 162.

D.M. 18 March 1998, Linee guida di riferimento per l'istituzione e il funzionamento dei Comitati Etici, Off. Gazz. 21/5/1998, No.122.

D.L.gs 24 June 2003, No.211 Implementation of directive 2001/20/EC relative to the application of good practice in carrying out clinical trials on drugs for medical use, Off.Gazz. No. 184 of 9-8-2003, Suppl. Ordinario No.130.

D.M. 17 December 2004 - Rules and conditions of a general nature, relative to the carrying out of clinical drug trials, with particular reference to those for the propose of the improvement of clinical practice, as an integral part of healthcare, Off. Gazz. 22 February 2005, No.43.