

Ethical aspects of medical publications Clinical assays on biological agents

When I was invited to write an article on this subject, my first impulse was to refuse; my mood quickly went from fear to modesty. How could I write about ethics without describing myself, my faults and transgressions, the most elementary, that I most certainly incur on the course of my duties. However, I then realized that my faults were not much greater or smaller than those of my colleagues.

Jaime Woolrich

President of the National Medical Academy of Mexico; 1979

I accepted such an honorable invitation since I had been, in the past, in charge of ethics at UNICAMP and of medical publications at the Presidency of the Commission on the Publication of Clinical Assays during the presidency of Hilton Seda (JAMB, AMB Journal. Year XI, #442, May 19, 1968, SP). But I only accepted it after asking myself if I have been ethical throughout my life and consoling myself with what Jaime Woolrich had said. Fortunately, unlike conscience, medical ethics changes from time to time, and among many examples, I should mention artificial insemination, which, more than half a century ago was not considered ethical, differently from the publicly accepted surrogate mothers, etc. Abortion, which has been condemned for centuries and currently is under discussion in the higher tribunals of the country, is a more significant example. Euthanasia, formerly condemned for representing a transgression of the most sacred Christian principles (God gave us life and only Him has the right to take it away), is currently practiced, reservedly in some European countries and openly in others. Both, euthanasia and abortion, were also condemned by Hippocrates and his disciples in 460 B.C., according to the Hippocratic Oath taken by physicians “I will

neither give a deadly drug, nor will I make a suggestion to this effect. Similarly, I will not give to a woman an abortive drug, etc.”

Four decades later, reviewing those regulations of the Commission on Clinical Assays, I cannot hide my disappointment and a certain dose of naiveness at that time, as, nowadays, medical offices are constantly invaded by publications, journals, fascicles, bulletins, Medical Societies journal, and etc. However, fascicles and like materials, containing a few pages dedicated to a specific drug, obviously with good response, clearly demonstrate the conflict of interest of the author who shows a certain methodological bias. The new Ethical Code has one article related to this matter. The physician should “art.109 – As a teacher or author of scientific publications He/she should oversee the veracity, clarity, and impartiality of the information presented, as well as declare any relationship with pharmaceutical, orthosis, prosthesis, equipment, implants of any nature, and other industries that might configure conflict of interest, even if it is a potential one.” In the chapter regarding: “Fundamental principles ´article XXIII – When involved in the production of scientific knowledge, the physician will be impartial and independent, aiming at the greater benefit for patients and society.” An inquiry carried out long ago, showed a surprising result, in that journals and those fascicles represented, after medical books, the second most common source of consultation for physicians. I dare say that, if this inquiry were undertaken nowadays, physicians would most certainly indicate them firstly, as very few physicians have private medical libraries or they are not available to all, and if they were, they would not have time for lengthy consultations in medical textbooks. Despite the shallowness with which the Internet approaches different subjects, it is currently the greater source of consultation, both fast and effective, even for patients who usually undertake an authentic battle of knowledge during office appointments.

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Except for those fascicles, which are not up for us to control, maybe other non-societal organs, but equally competent, such as the Regional Medical Board, the Ethics Commission of the Paulista Medical Association, or even ANVISA (the Brazilian equivalent of the FDA), could contribute to this. In my understanding, the latter, among all of them, has more responsibility for overseeing: quality of drugs; their pharmacokinetics and pharmacodynamics; the pertinent bibliography that attest the scientific reputability of the author; the hospital department he/she belongs to and whether it is trustworthy; and lastly, whether it was approved by the Ethics Commission of universities and departments for the promotion of excellence in clinical trials. We should not forget that fascicles, as a source of consultation, are also seductive, not to mention a partnership that the sales force of some pharmaceutical companies, a minority, surreptitiously expect from physicians to prescribe their drug in exchange of favors.

What has been said about those fascicles also applies to journals, as a source of information of Medical Societies, but with more stringency, as we carry on our shoulders an immense responsibility to determine what is ethical and what is not. We live under the same medical ethics, without the most remote possibility of separating ethics in the practice of medicine from the one in physician's field and, therefore, apply also in medical publications. Influenced by them, physicians with a poor information supply, located in places far from large centers, with communication difficulties, could endanger a large population. Note that patients, and not physicians, are the ones endangered by the effects of drugs. They do ask us whether they are being used as guinea pigs, and I believe they are, because each patient represents a new accumulated experience. When biologicals were introduced in the treatment of rheumatic diseases, they were greeted with great enthusiasm and, only later, it became known that they were more effective when used in association with methotrexate or leflunomide, but did not always present a good response, and there were cases which required the use of another biological agent. It has always been the same for other medications, among them corticosteroids and, more recently, anti-COX2 drugs.

As for the publication of clinical trials, I do not consider them to be different from others. However, the expression "conflict of interest", which by definition refers to situations in which economical or other aspects of personal interest could compromise or appear to compromise the judgment or decision of a professional in his administrative, managerial, teaching, research, assistance, or other activities, was created several years ago. Therefore, it does not apply only to merely economical aspects. Personally, I cannot distinguish an ethical from a possible non-ethical article because I assume that the latter would not be approved by a competent editorial board, as it would jeopardize the probity of the said journal, according to an old French saying – *il ni a pas de science sans conscience*. Thus, medical journals have an impact, to a lesser or higher degree, depending on their scientific level. As an example, I could mention the Lancet, the New England Journal of Medicine, Arthritis and Rheumatism, Annals of Rheumatic Diseases, Annals of Internal Medicine, and etc. As a matter of fact, they have been publishing clinical trials, especially on this new class of drugs, the biological agents. When I stated that the concept of ethics is mutable, I also recall mentioning conscience, which is not and has a literally absolute character and it is in no way subordinated to any type of conflict of interest. Note that when a Clinical Trial is submitted to the Editorial Board of the Brazilian Journal of Rheumatology, it has presumably been assessed by several ethical and scientific borders, from isolation of a molecule to *in vitro*, *in vivo*, and *ex-vivo* assays, phase three in *anima mobile*, and so forth. The Pharmaceutical Industry is the most interested of all in verifying the efficacy and tolerability of a drug and the drugs that do not meet those requisites can cause irreparable damage in the form of indemnifications, suspended profits, a fall in their stocks, etc. We have already mentioned all other frontiers and, in summary, like international borders, I cannot see the inconvenient in publications of any nature, investigational, observational, and clinical trials, as long as they are ethical and dictated by one's conscience. Regulation of their publication is mandatory.

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