ICH-GCP e Dichiarazione di Helsinki

Bibliografia

(cliccare sui titoli per aprire l'articolo originale)

Goodyear MDE, Lemmens T, Sprumont D, Tangwa G. “Does the FDA have the authority to trump the Declaration of Helsinki?” (BMJ 2009; 338: b1559)

The Food and Drug Administration (FDA) of the United States has ruled that clinical trials performed outside the US no longer have to conform to the Declaration of Helsinki if used to support applications for registration of products in the US. Instead, the International Conference on Harmonisation Good Clinical Practice (GCP) has been designated as the new regulatory standard. This suggestion met considerable opposition from scientists, ethicists, and consumer groups before and during the consultations. The FDA’s justifications included the arguments that it was merely harmonising its regulations with a global standard, and that legal instruments, such as the US Code of Federal Regulations, cannot embed external documents subject to change beyond the agency’s control (dynamic referencing).

“Trials on trial” (Nature 2008; 453: 427-8)

Later this year, the US Food and Drug Administration (FDA) will adopt new standards for human clinical trials conducted without its advance sign-off in foreign countries. The rules will govern whether data from such trials can be used in applications to market the drug in question in the United States. Although these new standards specify how to run such trials to meet US requirements, they are worryingly silent on key issues relating to human rights, in contrast with the rules currently in effect. As a result, they could open the way to some ethically fraught decisions.


In October 2008, the 59th World Medical Association (WMA) General Assembly in Seoul adopted the 7th revision of the Declaration of Helsinki: “Ethical Principles for Medical Research Involving Human Subjects.” This new version is the result of an extensive review process which started in 2007 and which received contributions by various national medical associations, researchers, and medical journal editors (1). The 7th revision of Declaration contains important new requirements related to the registration of clinical trials and reporting of their results.


Since 1964, the Declaration of Helsinki has stood as one of the world's most authoritative statements on ethical standards for human research. Drafted by the World Medical Association to provide medical researchers with ethical guidance, the Declaration has undergone six major revisions, most recently in October, 2008. For many years the US Food and Drug Administration (FDA) has required that foreign clinical studies supporting applications for drug licensure comply with the Declaration. However, on Oct 27, 2008, the FDA formally discontinued its reliance on the Declaration and substituted the International Conference on Harmonization's Guideline for Good Clinical Practice (GCP).
Four years ago, the US Food and Drug Administration (FDA) ceased compliance with the Declaration of Helsinki (DoH) (2000 revision and all subsequent revisions) for conduct of clinical trials outside its borders. It instead ruled that compliance with the Good Clinical Practices (GCP) of the International Conference of Harmonization (ICH) is sufficient. However, the ICH-GCP guidelines do not address certain ethical requirements stipulated in the DoH, such as the use of placebos v. standard therapy, post-trial access to treatment and other benefits for participants; public disclosure of trial design; publication of trial results; and disclosure of conflicts of interest. The FDA's adoption of less morally stringent guidelines could encourage pharmaceutical companies to take ethical short cuts. It could also have practical consequences for trial ethics in developing countries, especially where research ethics committees may not be promoting high standards of protection for participants in clinical trials, due to lack of financial and human resources. Pharmaceutical companies may also pressurise research ethics committees to relax guidelines and legislation, in order to facilitate future clinical trials in developing and emerging countries that lack the resources to conduct their own clinical research on epidemics such as HIV/AIDS, which have devastating effects on their populations.

Lang T, Siribaddana S “Clinical trials have gone global: is this a good thing?” (PLoS Med 2012; 9(6))

The United States Food and Drug Administration (FDA), for example, rejected the declaration’s 2000 and later revisions, largely over the question of whether placebos should be allowed in clinical trials in resource-poor settings, says Lemmens. In 2006, the FDA announced it was adopting the Good Clinical Practice standards developed by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use as its ethics guide for clinical trials. Unlike the declaration, which was drafted by physicians for physicians, those standards are developed by regulators in Japan, the US and Europe, in conjunction with the pharmaceutical industry.


The Declaration of Helsinki has been revised six times since then and has had an influence on international policy for many years. However, a 2000 revision of the declaration was rejected by both the U.S. Food and Drug Administration (FDA) and Canada’s Therapeutic Products Directorate (TPD), the two national drug regulators. The FDA and TPD instead chose to endorse the International Conference on Harmonisation’s Guideline on Good Clinical Practice, whose document E-10 (ICH E10), explicitly permits the use of placebo, even when proven effective treatment is available (Kimmelman,Weijer, and Meslin 2009). The reasons behind this move away from Helsinki are in part political (Sampson, Weijer, and Pullman 2009), but the overarching thrust of the arguments against Helsinki’s restriction of placebo controls, and against clinical equipoise as an ethical requirement, assert that there exists a conflict between the ethical and epistemic needs of clinical research.


This article examines issues relating to ethics decision-making in clinical trials. The overriding concern is to ensure that the well being and the interests of human subjects are adequately safeguarded. In this respect, this article will embark on a critical analysis of the ICH-GCP Guideline. The purpose of such an undertaking is to highlight areas of concern and the shortcomings of the existing ICH-GCP Guideline. Particular emphasis is made on how ethics committees perform their duties and responsibilities in line with the principles outlined in the ICH-GCP Guideline. This article will draw attention to the need for a new approach to addressing the weaknesses of the ICH-GCP Guideline in its present form.

Within the European Union (EU), good clinical practice (GCP) provides an ethical mandate to regulators; however, it is unclear what the content of that mandate is. By looking at the correspondence between GCP and ethical imperatives, we identify that the mandate is within the following: principles; benefit-risk ratio; scientific validity; results publication; informed consent; respect for participants; and special populations. There are also cases when regulations were ethical but were not pairable to an imperative, and when the former were stricter than the latter. Hence, we suggest closer cooperation between ethics committees and regulators to ensure that future versions of ethics guidelines cover the ethically relevant regulations that were not directly pairable to any imperative, and cooperation between GCP legislative bodies and ethics guideline-making bodies to resolve the discordant areas.