

Guide for Clinical Trial Staff

The 'Guide for Clinical Trial Staff' is based on the Good Clinical Practice Guidelines developed by the International Conference on Harmonization, which was attended by health authorities and pharmaceutical industries of Japan, the US and Europe. The book provides an universal introduction to the international standard, which together with the requirements of the country where the study is being conducted makes up the rules to be followed.

Good Clinical Practice

During the 18th World Medical Assembly in Helsinki in 1964, the World Medical Association adjusted the Nuremberg Code to the needs of the biomedical community. They produced the first version of the recommendations guiding physicians in biomedical research involving human subjects, better known as the Declaration of Helsinki, which is still the main basis for ethical issues in clinical trials.

The Declaration of Helsinki prompted several bodies to prepare guidelines regarding good clinical practice.

The first GCP guidelines ready to be implemented were developed by the FDA between 1977 and 1981. In 1982, the Council for International Organizations of Medical Sciences (CIOMS) - under the auspices of the WHO and UNESCO - published the "Proposed International Guidelines for Biomedical Research Involving Human Subjects", and in 1990, the Committee for Proprietary Medicinal Products of the European Community (CPMP) passed the "Note for Guidance: Good Clinical Practice for Trials on Medicinal Products in the European Community". These guidelines became effective in July 1991 and were gradually integrated into national law in Europe. Canada and the Nordic Countries (Scandinavia) had already implemented GCP in 1989, Japan had done so in 1990, and Australia in 1992.

However, differences in registration requirements among various countries (especially the 3 world markets Japan, US and Europe) led to repetitious experiments and trials, thereby considerably increasing costs, delaying the development, and, finally, the registration of drugs.

It became obvious that an international standard regarding quality, safety and efficacy was called for to reduce costs and increase efficiency in drug development.

In 1989, the health authorities and the pharmaceutical industries of Japan, the US and Europe agreed to work together on the harmonization of their technical requirements regarding the registration of new products. The International Conference on Harmonization (ICH) was initiated to provide a forum for a constructive dialogue between the regulatory authorities and the pharmaceutical industry.

Expected implications, besides facilitated registration procedures within the triad, include earlier availability of new treatments for patients as well as preservation of resources on the way to market approval. The necessity to duplicate pre-clinical and clinical studies

because of quality differences should become superfluous and, therefore, fewer humans and animals would be exposed to stress factors and risks.

It is worth mentioning that the representatives participating in the ICH process are evenly distributed between the pharmaceutical industry and regulatory authorities.

The task of the ICH Expert Working Group E6 was to harmonize the quality requirements of clinical trials by developing standardized GCP guidelines. After acceptance by the Steering Committee on May 1, 1996, the Consolidated Guideline for GCP was recommended for adoption by the regulatory authorities of the three regions. On July 17, 1996, this guideline was accepted in the European Union by the Committee for Proprietary Medicinal Products (CPMP) and came into operation on January 17, 1997, as a Note for Guidance. It replaced the EC Note for Guidance III/3976/SS-EN for GCP of July 1, 1991. In a next step, the pharmaceutical law in Japan was amended to comply with the ICH guideline on April 1, 1997. In the US, the ICH guideline was published in the US Federal Register as an official FDA guideline in May 1997. In Europe, the guideline was given out as a directive, i.e. it went through the review and approval processes of the European Parliament and the Council of Ministers. On December 12, 2000, the European Parliament voted in favor of the proposed directive on the implementation of GCP, which was then approved by the Health Council of the Council of Ministers on December 14, 2000, and published in the Official Journal of the European Communities on May 1, 2001.

It is important to understand that the directive itself is not a law that individuals can comply with. It only requires that EU member state governments incorporate the policies contained in the directive into their own national law.

Any sponsor or clinical investigator must of course comply with the national laws dealing with biomedical research. As a matter of fact, this has been the case already prior to implementation of the directive.

The 'Guide for Clinical Trial Staff' is intended as a universal introduction to the international standard based on ICH GCP which encompasses all aspects that need to be considered in conjunction with any local requirements of the country where the study is being conducted. Thus, specific items must be seen in analogy to the requirements as they might be outlined in any local regulation.

Gerhard Fortwengel
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