

APPLIED CLINICAL TRIALS

CLEAR: An EU Postgraduate Training Program

This new course aims to provide clinical research physicians with good clinical practice knowledge.

Jul 1, 2006

By: [Barbara Miletzki](#), [Christoph H. Gleiter](#)

Applied Clinical Trials



Investigators within the European Union who plan to design, conduct, record, and/or report clinical trials with medicinal products have to meet the principles of good clinical practice (GCP). All drug trials involving human subjects must be scientifically sound and guided by internationally recognized ethical principles to protect the rights, safety, and well-being of clinical trial participants. The Clinical Trials Directive 2001/20/EC¹ and the Good Clinical Practice Directive 2005/28/EC,² developed over the last few years, are two

European directives that support the ethical principles of good clinical practice.

Before these principles of good clinical practice were incorporated into the European legislation, they were developed as guidelines for the International Conference on Harmonisation (ICH)³; the ICH brings together the regulatory authorities of Europe, Japan, and the United States and experts from the pharmaceutical industry in the three regions. This ICH-GCP Guideline was developed in order to provide a unified standard for clinical drug trials taking place in the EU, Japan, and the United States. The objective of such a harmonization was to facilitate the mutual acceptance of clinical drug trial data by the regulatory authorities in these three jurisdictions. The guideline was created to reduce or even obviate the need to duplicate preclinical and clinical testing of new medicines and to use human, animal, and material resources more economically. Furthermore, the guideline was compiled to eliminate unnecessary delay in the global development and availability of new medicines and to maintain at the same time safeguards on quality, safety, and efficacy and regulatory obligations to protect public health. The ICH-GCP Guideline was subsequently adopted by the European Medicines Agency (EMA),⁴ and the principles of good clinical practice were incorporated in the previously mentioned directives.^{1,2}

Since the incorporation of the guidelines in European directives and their subsequent mandatory implementation in the national legislations of the individual member states of the EU, they are legally binding throughout the European Union.

This is a new situation, especially for clinical researchers who conduct noncommercial clinical drug trials without the participation of the pharmaceutical industry, otherwise also referred to as investigator-initiated trials (IITs). These clinical investigators, who mainly work at university hospitals and private practices, constitute a large group of physicians who need to be trained and educated in order to be able to apply the principles of good clinical practice in IITs to the full extent. Hari

It is important to know that the "Good Clinical Practice Directive" literally demands that "each individual involved in conducting a trial shall be qualified by education, training, and experience to perform his tasks." ² Moreover, the directive reads that the ethics committee, when making up its opinion on a clinical trial, "shall consider in particular [...] the suitability of the investigator and the supporting staff."

1

The principles of good clinical practice have been established to set an international standard for clinical drug trials. However, it is sensible to apply their methodology also—where applicable—to other clinical investigations (e.g., trials on surgical and diagnostic procedures) in order to safeguard the well-being of human subjects and the quality of data. It is advisable to do so because no comparable principles have been developed yet for other types of clinical research. Thus, even clinical researchers who want to investigate other problems or questions

other than medicinal products would be wise to become familiar with the principles of good clinical practice.

In summary, there is now an increased need for training opportunities with respect to the highly complex field of clinical research in the European Union—no matter whether clinical trials with or without investigational medicinal products are concerned. In order to fill this gap, the EU project CLEAR (clinical research physician) was created. Within this project, a European-wide, uniform postgraduate training program for clinical investigators has been developed. Its purpose is to impart the necessary knowledge about GCP, including a great variety of useful and helpful tools like biometrics and statistics or clinical and preclinical basics. The CLEAR project is now entering the phase of first pilot courses and will be further described below.

Project partners

Thirteen partners from the following seven European countries participate in this EU project: Austria, Cyprus, Germany, Greece, Hungary, Ireland, and Latvia.

The expertise that the different CLEAR partners bring with them into the project range from teaching, preclinical and clinical research, biostatistics, postgraduate training and seminar activities (e.g., courses for clinical investigators⁵ organized by the Coordination Centre for Clinical Trials at University Hospitals Tübingen and Ulm—KKS-TU GmbH, formerly KKS-UKT gGmbH) to didactical and methodical experience, as well as the capacity to realize eLearning concepts. Furthermore, the knowledge of various partners in the fields of quality assurance, accreditation of postgraduate education, national and international dissemination strategies, marketing, business development, and international project management is important for the success of the project.

Scientific advisors

The work of the CLEAR team is accompanied by an independent scientific board. The members of the board are experienced scientists who come from several European countries. They support the development of the project and ensure that the CLEAR team provides up-to-date, scientifically sound and quality-assured training materials.

Project financing

CLEAR is financially supported by the European Commission's vocational training program "Leonardo da Vinci." This program promotes transnational projects based on cooperation between the various participants in vocational training in an effort to increase mobility, foster innovation, and improve the quality of training. It is a key instrument in the drive to implement lifelong learning strategies that offer synergies between European policies for training and employment.⁷

Targeted group



Table 2. Contents of Module "Planning and Organization."

Curriculum content

The CLEAR course is intended for all physicians and other persons who want to perform clinical research involving human subjects irrespective of the type of clinical study. Although CLEAR is particularly suitable for investigators concerned with clinical drug trials since the emphasis of the training program is on the principles of good clinical practice, CLEAR is also of great value for researchers performing clinical trials other than drug trials. That is because the methodology for clinical drug trials is the best one developed and can therefore be used as a model for all other sorts of clinical trials—where applicable—for the reasons explained above.

CLEAR offers an excellent opportunity to gain the required theoretical knowledge and take an important step forward in acquiring the necessary qualification as clinical research physician—which, in addition to theoretical knowledge, also demands a certain amount of experience in performing clinical research tasks.

The content of the CLEAR curriculum covers all major topics relevant for investigators responsible for or collaborating on all



Table 1. Contents of Module "Preclinical and Clinical Basics."



Table 3. Contents of Module "Law and Ethics."

Table 4. Module "Statistics and Biometrics" contents.

sorts of clinical trials, with the main focus on clinical drug trials. The many complex aspects of clinical trials covered in the CLEAR course are structured into four modules: Preclinical and Clinical Basics, Planning and Organization, Law and Ethics, and Statistics and Biometrics. Tables 1–4 describe the curriculum contents of each module.

Table 3. Contents of Module "Law and Ethics."

Learning method

The content of the CLEAR curriculum is implemented via the so-called blended-learning method, which combines traditional face-to-face seminars with eLearning. In the case of the CLEAR course, a CD-ROM has been developed to deliver the learning program.

Table 5. Institutions and members of the CLEAR team.

The structure of the CLEAR CD-ROM mirrors the four modules of the curriculum. For each of the modules there is a section with detailed background information, which allows the user to either acquire new knowledge or deepen existing knowledge or to look up something quickly to solve a specific question. All texts are illustrated with loads of examples to make complex issues more understandable. In addition, a three-part library containing literature references, online resources, and a glossary can be consulted. In order to enable the learner to check his or her own knowledge and to create references to real-life situations, a large number of case studies is incorporated. Furthermore, a great variety of interactive exercises are awaiting the user. They range from multiple choice questions over drag and drop tasks to cloze exercises.

The fact that part of the CLEAR curriculum is imparted via eLearning enables CLEAR participants to work through the four modules at their own pace, as often as they like and whenever it suits them. The obvious advantages of eLearning will certainly be valued by the target group of CLEAR, which mainly consists of hospital and private practice physicians, who on the one hand have high professional standards and are used to studying on their own, and who on the other hand frequently lack the time for attending a lecture series or week-long seminars for further professional training.

Nevertheless, parts of the CLEAR curriculum are taught in classic face-to-face lessons to achieve optimal learning results. The presence of a lecturer and other course attendees can enhance the pleasure of learning and encourage the participants to ask questions or to discuss with each other. Thus, the advantages of eLearning are complemented by the advantages of face-to-face seminars in the CLEAR course.

Course languages

All eLearning materials of the CLEAR course are currently available in two languages: German and English. The English version of the CD-ROM has been produced to allow its use in all European countries no matter the native language.

Since the face-to-face seminars can be taught in whatever language is desired, the CLEAR course is truly multilingual.

Outcome assessments

At the end of the CLEAR course, the participants have to pass a written final examination in order to get a certificate of attendance. This test serves to check the knowledge acquired during both the face-to-face classes and the eLearning lessons.

Outlook and future plans

Due to the good results of the pilot courses, it has been decided to further develop this unique European, multilingual, postgraduate training program for clinical research physicians. In order to increase the possibilities of CLEAR, plans are underway to transform the eLearning parts from the computer-based program to a Web-based training program. In addition to such advantages as more interactivity between participants and tutors, this will facilitate the necessary continual updating of the contents. The CLEAR project homepage provides continuously updated information on its current status.⁶

CLEAR team members

The institutions (and members) of the CLEAR team are listed alphabetically in Table 5.

Acknowledgement

The CLEAR project is financially supported by the European Union (Agreement No 2003-A/03/B/F/PP-158.023).

References

1. European Parliament and Council of the European Union, "Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations, and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use," *Official Journal of the European Union*, 44, L121/34–44 (2001).
2. Commission of the European Communities, "Commission Directive 2005/28/EC of 8 April 2005 laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing and the importation of such products," *Official Journal of the European Union*, 48, L091/13–19 (2005).
3. Guideline for Good Clinical Practice, ICH guideline, efficacy topic E6, available at: www.ich.org/ (last accessed January 2005).
4. Note for Guidance on Good Clinical Practice, CPMP/ICH/135/95, adopted July 96, available at: www.emea.eu.int/ (last accessed January 2005).
5. K. Schaber, C. Beckmann, C. Brochhausen, K. Mörike, M. Schwab, H.W. Seyberth, and C.H. Gleiter, "Arzneimittelprüfungen in der Pädiatrie," *Arzneimitteltherapie*, 22, (5) 150–153 (2004).
6. CLEAR—Clinical Research Physician: www.euclear.com/new/front.aspx (last accessed December 2005).
7. The European Commission's Leonardo da Vinci program: www.europa.eu.int/ (last accessed December 2005).

Barbara Miletzki is with the Coordination Centre for Clinical Trials at University Hospitals Tübingen and Ulm, Tübingen, Germany. **Christoph H. Gleiter*** is also with the Coordination Centre for Clinical Trials at University Hospitals Tübingen and Ulm, KKS-TU GmbH, Otfried-Müller-Str. 45, 72076 Tübingen, Germany, +(49) 7071 29-72262, fax +(49) 7071 29-5158, email: christoph.gleiter@kks-tu.de, as well as the Department of Clinical Pharmacology, Institute of Pharmacology and Toxicology, University Hospital Tübingen.

*To whom all correspondence should be addressed.