GUIDELINE ON THE PRINCIPLES OF TRAINING PROGRAMMING AND EVALUATION IN CLINICAL TRIALS 13 NOVEMBER 2015

1. PURPOSE This guideline has been prepared to provide guidance on the form and content of the application to be made to the Turkish Medicines and Medical Devices Agency (TİTCK) regarding training programs planned to be organized on good clinical practice and clinical trials.

2. BASIC PRINCIPLES 2.1. The number of participants attending the training should be limited to a minimum of 20 and a maximum of 80 persons. However, this limitation does not apply when distance learning is planned. 2.2. At least two workshop sessions appropriate to the nature of the training should be conducted. However, when distance learning is planned, at least two video presentations should be included. 2.3. If appropriate for the planned training program, at least one role-play video presentation should be included. 2.4. The venue where the training is delivered should have internet-connected laptop computers, projection equipment, a DVD or VCD player, and an audio system (including a lavalier microphone). 2.5. At least one (1) "question-and-answer exercise", preferably supported by computer software, should be conducted. 2.6. It is preferable that the physical venue where the training will be held be structured as one large hall with tables arranged in a classroom-style seating layout and, when necessary, convertible into two small halls. 2.7. Throughout the course, there should be a course coordinator who is proficient in the subject and able to answer any administrative and educational questions of the participants.

3. IMPLEMENTATION 3.1. Throughout the training, a quality assurance officer proficient in the subject should evaluate the trainer's presentation, his/her capacity to answer questions asked, and his/her attention to the trainees. 3.2. At the beginning of the training, the expectations of the participants should be queried. 3.3. At the beginning of the training, a pre-test of at least 10 (ten) questions should be administered to measure the knowledge level of the participants. 3.4. Attendance obligation for the training should be set at a rate of 3⁄4 per session. 3.5. Preferably at each presentation, and where this is not possible at each session, the signatures of the participants should be recorded. 3.6. Each participant should be given a name badge, a program, course notes, and additionally a notepad and a pen. 3.7. In trainings lasting more than one day, a summary of the previous day's training should be made at the start of the second day. 3.8. Before starting advanced-level trainings organized following the basic training, a reminder of the information provided in the basic training should be given, and only those who have been successful in the basic training should be included in the advanced-level training program. 3.9. Presentations in the training should not exceed 45 (forty-five) minutes, and workshop sessions should not exceed 3 (three) hours. 3.10. Preferably, the trainers involved in the training should attend throughout the duration of the training.

4. EVALUATION 4.1. Evaluation activities should be carried out under two headings: "assessment of participants' success" and "evaluation of the training program". 4.1.1 Assessment of participants' success: At the end of the training, the participants' success should be assessed by means of an examination of at least 10 (ten) questions, and a "certificate of achievement" should be given to those whose attendance is appropriate and who are found successful, and a "certificate of attendance" to those who fail the examination. In order for a certificate of achievement to be issued, the passing grade must be at least 70 (seventy). 4.1.2 Program evaluation: In order to evaluate the effectiveness of the training program, feedback should be obtained from the participants.

4.2. A "certificate of achievement" or "certificate of attendance" must bear the signature of the course coordinator. 4.3. These trainings should be repeated at appropriate intervals, and, if requested by the Turkish Medicines and Medical Devices Agency, the certificate of achievement obtained at the end of the training should be renewed.

5. TRAINERS 5.1. Trainers should, depending on the nature of the subjects, have received a training on clinical trials and good clinical practice that is valid (approved by the Turkish Medicines and Medical Devices Agency) and should be selected from among persons who are experts in their

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field. 5.2. Trainers other than faculty members must have completed a "training of trainers" program and must document this.

6. REQUIREMENTS FOR THE DISTANCE LEARNING PROGRAM 6.1. All matters specified in this guideline that are applicable also apply to the distance learning program. In addition, at least the matters specified below must be fulfilled: 6.1.1. Distance learning programs may be delivered via websites to be established specifically for the training by the Ministry of Health and its Affiliated Organizations, Universities, Gülhane Military Medical Academy, Training and Research Hospitals, and relevant Associations and Foundations that are directly related to the subject. 6.1.2. The basic structure of the training should be configured as training programs, training modules, assessment questions, and feedback. Each module should be composed of written, audio, and visual elements addressing one subject. 6.1.3. The website on which the training will be delivered must not contain any statement or announcement that would include advertising unrelated to the subject, other than the logo and name of the institution or private organization. 6.1.4. The institution that will deliver the training, the training subject headings, and the trainers delivering the training should be clearly indicated on the website where the training will be held. 6.1.5. It should be clearly stated on the home page that the program is approved by the Turkish Medicines and Medical Devices Agency. Training programs that do not have Turkish Medicines and Medical Devices Agency approval may not be delivered or certified. 6.1.6. All users who will use the system must be registered. For this purpose, a registration form must be completed. The information to be collected in the registration form (first name, surname, Turkish national identification number, e-mail address, city and country of residence, profession, field of expertise, duration of work in the field of expertise, institution of employment, position, institution address, telephone, mobile phone) should also query the user's eligibility for access to this system. The user must confirm the accuracy of the information provided. After entering the user information, the user should read the rules stating the purpose of use and confirm that he/she has read and understood them. 6.1.7. A confirmation e-mail containing the temporary account information should be sent by the system to the user whose registration is approved. The user should enter the account information sent to him/her into the system and should be required to update his/her password for security reasons. 6.1.8. In accordance with the sequence of the training modules constituting the certification program, the prerequisites of each module should be as follows: 6.1.8.1. One should not proceed to the second module without obtaining a passing grade from a training module. 6.1.8.2. At the end of each module, a passing grade consisting of the evaluation of the answers to the questions asked in that module should be calculated. The passing grade should not be below 70 (seventy). 6.1.8.3. The user should take the modules and assessment tests in accordance with the designated certification program. 6.1.8.4. If a user who has started a training module included in the certification program exits the system before completing the module, upon re-entering the system, he/she should be able to continue the relevant training from where he/she left off.

6.1.8.5. The user lists the training modules included in the certification program that he/she has completed, has started but not completed, and has not yet started. For each module, he/she sees how much time was spent, how long it took to complete, and the date of completion. For modules started but not completed, he/she sees the percentage completed. 6.1.8.6. The user views his/her status in the examinations at the end of each module, tracks his/her answers to the questions and his/her success status. 6.1.8.7. Each program must be completed within a maximum of 6 (six) months, and each module within a maximum of 1 (one) month. Where this cannot be achieved, a period of 12 (twelve) months must elapse before he/she can reapply for the program. 6.1.8.8. The user answers the end-of-module survey for each training module and submits, if any, his/her comments on the module. Comments written for the module are approved by the module instructor or the site administrator, responded to if necessary, and then made visible to other users. 6.1.8.9. The user may rate the module he/she has completed. 6.1.8.10. The user may follow

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a module; when other users submit comments on the relevant module, he/she is notified accordingly. 6.1.8.11. A user who completes the certification program in accordance with the determined criteria is notified by the system that he/she has successfully completed the program, and is informed via e-mail. The user who completes the certification program is provided with the certification prepared for printing or downloading and approved by the Turkish Medicines and Medical Devices Agency (TİTCK). 6.1.9. The objectives and intended targets of each module are determined and stated in writing at the beginning of the module. 6.1.10. The time spent in the module by each participant and by all persons attending each year, the answer success rate in each module, their overall success rates, and module feedback notes and assessments are evaluated by a "Quality Assurance Officer" throughout the training. 6.1.11. All activities of the users in the e-learning system are recorded. 6.1.12. As of the date the user registers in the system, the date of each login and the activities performed after each login are kept and reported by the system. 6.1.13. The status of the user in each training module included in the certification program is reported. Start and completion dates, total time spent in the module, and the score obtained in the end-of-module test are reported. 6.1.14. Users who have started, completed, or are continuing each module, as well as users who have completed the certification program, are listed. 7. APPLICATION AND PERMIT 7.1. In accordance with the application form and cover letter template published on the website of the Turkish Medicines and Medical Devices Agency (TİTCK), the application must be made to the Agency at least one month prior to the start date of the training program. Arrangement approval is granted to those found suitable as a result of the review carried out. 7.2. The training must not be conducted without a permit from the Agency. 7.3. Trainings to be organized by the relevant associations and foundations, the pharmaceutical and medical device sector, and contract research organizations must be conducted in cooperation with the Gülhane Military Medical Academy, the Ministry of Health and its affiliated organizations, universities, or training and research hospitals. 7.4. The content of the presentations made during the application and the training to be conducted must comply with the relevant legislation in force in our country. 7.5. The application for distance learning programs must be made in two stages. The first stage is the pre-eligibility application stage for certification. At this stage, the content of the program, the program presenters, and the format of the program delivery must be clearly specified. Standard operating procedures related to the distance learning process must be attached to the application, and these must explicitly include quality control systems and implementation stages. If, at this stage, the Agency issues an eligibility decision for certification, the program content must be placed on a demo web page but must not be opened for use. In the second application made to the Agency, the opinion of the Agency must be obtained by submitting the final version of the program and the address of the demo web page, together with the login password for these pages. If a favorable opinion is received at this stage, the program may be opened for use, and in addition to the program certification, the certification approved or issued by the Agency may be provided to successful candidates in a password-protected and secure manner. 8. ADMINISTRATIVE SANCTIONS 8.1. Upon determination that a training has been organized or participation has been provided in a manner contrary to this Guideline and the relevant legislation, the applicant and the relevant persons are warned by the Agency. If the action in question continues after the date of the warning, the applicant may not organize any training for a period of 6 (six) months. 9. REPEALED PROVISIONS The "Guideline on Training Programming and Evaluation Principles Related to Clinical Trials and Good Clinical Practice", which was put into effect by the Approval No. 86401 dated 15.07.2014, has been repealed. The name of the Guideline has been changed to "Guideline on Training Programming and Evaluation Principles in Clinical Trials". 10. ENTRY INTO FORCE This Guideline enters into force on the date of its approval. 11. EXAMPLES OF TRAINING PROGRAMS The training programs specified below are given as examples. The course content may be modified in accordance with the course title. 11.1. Basic course program on the ethical approach in clinical trials 11.1.1. Duration of the Training: The duration of the training must be at least 1 and at most 4 days. 11.1.2. Target Audience: This training must be directed at ethics committee members and

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investigators. 11.1.3. Purpose: It is aimed at understanding the basic ethical approaches and principles in clinical trials. 11.1.4. Two separate modules may also be prepared: Scope of Module 1: The scope of the training may include the following topics. Philosophy and historical development of the ethical approach in clinical trials Ethical dimension of clinical trials National legislation in clinical trials Duties, authorities, and responsibilities of ethics committees Characteristics of ethics committees Establishment, function, and practices of ethics committees Characteristics that make a clinical trial ethical Misconduct in clinical trials Conflict of interest in clinical trials Statistical evaluation in clinical trials and reliability of trial results Ethics approval process Relations between ethics committee/investigator/sponsor/contract research organization Scope of Module 2: The scope of the training may include the following topics. Quality control and assurance in clinical trials Methodology in clinical trials Statistical approaches in clinical trials Safety reporting and evaluation in clinical trials Clinical trials in children Clinical trials in the elderly

Clinical trials in psychiatry and the use of placebo The ethical dimension of genetic research Ethical approaches concerning female volunteers in clinical trials Clinical trials in healthy volunteers Sources of error in different trial types The ethical dimension of observational studies Problems encountered in practice 11.2. Course programme on standardization requirements for the structuring of ethics committees 11.2.1. Duration of the Training: The duration of the course should be at least 1 and at most 4 days. 11.2.2. Target Audience: This training should be directed at ethics committee members. 11.2.3. Objective: It is aimed at understanding and evaluating the fundamental ethical approaches and principles in clinical trials. 11.2.4. Scope: The scope of the training may include the following topics. National legislation on clinical trials Fundamental principles of good clinical practice (GCP) The importance of the Declaration of Helsinki and the points to be complied with The historical development of ethical values in clinical trials Ethics committee structure and characteristics Ethics committee duties and responsibilities Bioethics and clinical trial ethics The ethics approval process Rights of volunteers/patients involved in clinical trials The importance of the informed consent form (ICF) and review of the ICF at application (workshop) The need for drug development and phases in clinical drug trials Statistical evaluation in clinical trials and the reliability of trial results General principles of quality management The definition of the "standard operating procedure", the reasons for its use and its content Preparation of a "standard operating procedure" document (workshop) Quality control and quality assurance in clinical trials Budgeting in clinical trials Review of the application dossier (workshop) Safety reporting in clinical trials Relationships between the ethics committee/investigator/sponsor/contract research organization Conflict of interest in clinical trials 11.3. Introduction/basic training on clinical trials 11.3.1. Duration of the Training: The duration of the training should be at least 1 and at most 4 days. 11.3.2. Target Audience: This training should be directed at investigators and sponsors. 11.3.3. Objective: It is aimed at understanding the fundamental principles in clinical trials. 11.3.4. Two separate modules may also be prepared: Scope of Module 1: The scope of the training may include the following topics. Fundamental principles of good clinical practice (GCP) The importance of the Declaration of Helsinki and the points to be complied with The new drug development process Terminology in clinical drug trials Terminology in non-drug clinical trials Observational studies Duties and responsibilities of the parties in a clinical trial Informing volunteers and the informed consent form

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Legal regulations Safety reporting Practices carried out by the local authority in accordance with the relevant legislation Scope of Module 2: The scope of the training may include the following topics. Clinical trial protocol Investigator's brochure Basic statistical concepts The concept of pharmacokinetics The concepts of pharmacogenetics and pharmacogenomics Quality control in clinical trials Protection of volunteers/patients and the Declaration of Helsinki Clinical

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trial design Methodology in clinical trials (such as blinding, randomization) Placebo control in clinical trials Project management in clinical trials Special parameters in clinical trials (such as quality of life) Data management (such as data collection, data entry, data validation) Data reliability/security 11.4. Monitoring in clinical trials 11.4.1. Duration of the Training: The duration of the training should be at least 2 and at most 3 days. 11.4.2. Target Audience: This training should be directed at sponsors and monitors. 11.4.3. Objective: It is aimed at understanding the fundamental principles of monitoring in clinical trials. 11.4.4. Scope: The scope of the training may include the following topics. Monitoring policy Legal regulations in clinical trials Introduction to good clinical practice (GCP) Introduction to good laboratory practice (GLP) Quality assurance and standard operating procedures Terminology in clinical trials Essential documents of the trial file Misconduct in clinical trials Selection and characteristics of monitors Responsibilities of the monitor Reporting Data management (such as data collection, data entry, data validation) Data reliability Accounting for and destruction of investigational products 11.5. Clinical research nurse training programme 11.5.1. Duration of the Training: The duration of the training should be at least 2 and at most 3 days. 11.5.2. Target Audience: This training should be directed at clinical research nurses. 11.5.3. Objective: It is aimed at understanding the fundamental principles related to clinical trials. 11.5.4. Scope: The scope of the training may include the following topics. Terminology in clinical trials Legal regulations in clinical trials Definition of the trial and design phases Ethics committees in clinical trials Trial site management Research nursing

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Responsibilities in clinical trials Randomization and blinding in clinical trials Source documents in clinical trials The application process in clinical trials Tracking of investigational products Study close-out procedures Adverse event reporting 11.6. Advanced clinical trials training programme 11.6.1. Duration of the Training: The duration of the training should be at least 2 and at most 5 days. 11.6.2. Target Audience: This training should be directed at investigators, sponsors and persons employed in contract research organizations who have successfully completed the basic training. 11.6.3. Objective: It is aimed at understanding more specialized topics in clinical trials. 11.6.4. Scope: The scope of the training may include the following topics. Data management in clinical trials Risk management in clinical trials Volunteer recruitment and retention of volunteers in the study Trial types directed at specialized topics such as oncology studies and psychiatry studies Evaluation of statistical data Translational studies Pharmacogenetics and pharmacogenomics Causality assessment in safety reporting Scales used in trials and their evaluation Protocol writing 11.7. Research pharmacist training programme 11.7.1. Duration of the Training: The duration of the training should be at least 1 and at most 3 days. 11.7.2. Target Audience: This training should be directed at research pharmacists. 11.7.3. Objective: It is aimed at understanding the fundamental principles related to clinical trials. 11.7.4. Scope: The scope of the training may include the following topics. Terminology in clinical trials Legal regulations in clinical trials Definition of the trial and design phases Trial site management Duties and responsibilities of the research pharmacist Randomization and blinding in clinical trials Source documents in clinical trials Tracking and accounting of investigational products Study close-out procedures Adverse event reporting

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