Söğütözü Mahallesi, 2176. Sokak No:5 06520 Çankaya/ANKARA

GUIDELINE ON THE APPLICATION PROCEDURE FOR EFFICACY AND SAFETY STUDIES ON COSMETIC PRODUCTS OR RAW MATERIALS AND CLINICAL TRIALS

Telephone: (0 312) 218 30 00 Fax: (0 312) 218 34 60 E-mail: halkla.iliskiler@titck.gov.tr Website: https://www.titck.gov.tr Kep Address: titck@hs01.kep.tr

GUIDELINE ON THE APPLICATION PROCEDURE FOR EFFICACY AND SAFETY STUDIES CONDUCTED ON COSMETIC PRODUCTS OR RAW MATERIALS AND CLINICAL TRIALS KÜD-KLVZ-44

First Version Effective Date: 27.10.2015 1st Revision Effective Date: 15.11.2022

Purpose

ARTICLE 1- (1) This Guideline has been prepared pursuant to the requirements of the Regulation on Efficacy and Safety Studies and Clinical Trials of Cosmetic Products or Raw Materials, in order to provide guidance on the form and content of the application to be made to the Turkish Medicines and Medical Devices Agency for conducting efficacy studies, safety studies or clinical trials of cosmetic products or raw materials to be performed on volunteers.

Scope

ARTICLE 2- (1) This Guideline has been prepared for natural or legal persons who will conduct efficacy studies, safety studies or clinical trials with cosmetic products or raw materials on volunteers.

Legal Basis

ARTICLE 3- (1) This Guideline has been prepared based on the Regulation on Efficacy and Safety Studies and Clinical Trials of Cosmetic Products or Raw Materials, published in the Official Gazette No. 29481 dated 20/09/2015.

Definitions

ARTICLE 4- (1) In this Guideline; a) Informed consent form (ICF): refers to the document evidencing in writing the consent obtained by providing detailed and comprehensible information about the study or research, b) Study or research protocol: refers to the document that describes in detail the objective, methodology, statistical methods to be applied and arrangements of the study or research, of efficacy studies, safety studies or clinical trials of cosmetic products or raw materials, c) Sponsor: refers to the person, institution or organization responsible for the initiation, conduct or financing of efficacy studies, safety studies or clinical trials of cosmetic products or raw materials, ç) Cosmetics Clinical Trials Ethics Committee: refers to the independent committees to be established or approved by the Agency in order to provide scientific and ethical opinions on the study or research protocol, the suitability of the investigators, the adequacy of the premises where the study or research will be conducted, the methods and documents to be used in informing the volunteers, the consents to be obtained from the volunteers, and other matters related to the studies or research, with the purpose of ensuring the protection of the rights, health-related safety and well-being of the volunteers who will participate in the study or research to be conducted with cosmetic products or raw materials, and of ensuring that the study or research is conducted and followed up in compliance with the relevant legislation, ç) Agency: refers to the Turkish Medicines and Medical Devices Agency,

d) Principal investigator: refers to the person responsible for the conduct of the study or research, who has completed education at the level required by the study or research in the field

Unofficial English translation for information purposes only. In the event of any discrepancy, the Turkish original text (mevzuat.gov.tr) shall prevail.

related to the study or research, e) Contract research organization (CRO): refers to the independent organization to which the sponsor has transferred all or part of its duties and authorities related to efficacy studies, safety studies or clinical trials of cosmetic products and raw materials by means of a written contract,

Form and content of applications and notifications

ARTICLE 5- (1) The application shall be made, in compliance with the legislation, by the sponsor, the contract research organization to be appointed by the sponsor, or the principal investigator. (2) In order to conduct studies or research with cosmetic products or raw materials on volunteers, an application shall be made to the Department of Cosmetic Products of the Turkish Medicines and Medical Devices Agency. (3) The application must be made using the standard application form and cover letter template published on the Agency's website. The said forms are updated as necessary, and care should be taken to ensure that the form to be used in the application is up to date. (4) If the study or research is international, a list of other relevant authorities to which the same application has been submitted shall be attached to the file. If there are differences between the protocol and other matters to be implemented in other countries and the protocol and other matters to be implemented in our country, these shall be specified together with their justifications. (5) If the applicant is not the principal investigator or the sponsor of the study or research, the original of the document indicating the matters in which the contract research organization has been authorized by the sponsor shall be included in the application file. (6) For initial applications and applications for substantial modifications, the original and one copy of the bank receipt evidencing payment of the application fee published on the Agency's website shall be included in the application file. (7) No application fee payment is required for academic studies or research (thesis, project, etc.). However, a document approved by the head of the relevant institution (dean in faculties, secretary general or hospital director in hospitals), indicating that the study or research in question is for academic purposes, shall be included in the application file. (8) The sponsor, the contract research organization to be appointed by the sponsor, or the principal investigator, by signing the relevant application form, undertakes that the information submitted is sufficient, that the attached documents accurately reflect the existing information, that they consider it appropriate to initiate the study or research according to their own views, and that they accept the initiation of the study or research.

Unofficial English translation for information purposes only. In the event of any discrepancy, the Turkish original text (mevzuat.gov.tr) shall prevail.

Study or research protocol

ARTICLE 6- (1) The content of the study or research protocol shall consist of the following: a) Protocol title, protocol number and date, b) The number and date of the amendment in protocol amendments, c) The names and contact information of the sponsor, the contract research organization to be assigned by the sponsor, or the responsible investigator, ç) The name, title, address of the study or research site, and contact information of the investigators responsible for conducting the study or research, d) The objective, purpose and scope of the study or research, e) The name, specifications, safety assessment report, shelf life, storage conditions, stability, manufacturer and manufacturing information of the cosmetic products or raw materials used in the study or research, f) Information on the category, application site, method of application, amount of application, duration and frequency of use of the cosmetic products or raw materials used in the study or research, g) Packaging and labeling information of the cosmetic products or raw materials used in the study or research, ğ) A declaration that the study or research will be conducted in compliance with the protocol and the legislation, h) A definition of the volunteer population in which the study or research will be conducted, ı) Scientifically substantiated documents, including basic information about the study or research, i) The duration of the study or research, j) The design and methods of the study or research, k) The number of volunteers planned to be included in the study or research, l) In multicenter studies or research, the number of volunteers planned to be included for each center, m) The inclusion and exclusion criteria of volunteers for the study or research, n) The withdrawal criteria of volunteers from the study or research, o) Information on whether new volunteers will be enrolled to replace volunteers who

have withdrawn from the study or research, and if so, how this will be done, ö) Methods for reporting and recording undesired and serious undesired effects, p) Information on how and for how long volunteers will be followed up after undesired and serious undesired effects, r) Criteria for terminating the study or research, s) The statistical methods to be applied, ş) Information on the selection of volunteers to be included in the analyses, t) Information on the processing of data and the keeping of records, u) The criteria for the final evaluation of the study or research, ü) Information on the persons, institutions or organizations authorized to have direct access to source data, v) Information on funding and insurance. (2) The protocol submitted as an annex to the study or research file; shall include the version number of the protocol, the full title of the study or research, the code numbers of all versions of the protocol determined by the sponsor, the contract research organization to be assigned by the sponsor, or the responsible investigator, the version number and date to be updated with the inclusion of amendments, or the short title or name given to this protocol, and shall be signed by the sponsor, the contract research organization to be assigned by the sponsor, or the responsible investigator. (3) If the study or research protocol and the protocol amendment are in a different language, the original of the protocol shall be submitted together with the Turkish translation of the protocol and the protocol amendment. Notification of amendments and the authorization procedure

ARTICLE 7- (1) After a study or research has been initiated, amendments may be permitted during its conduct. (2) Significant amendments to be made regarding the study or research may not be implemented without the authorization of the Agency and the approval of the ethics committee. (3) The matters to be considered significant amendments in studies or research are: a) A change in the sponsor or the contract research organization to be assigned by the sponsor, b) A change in the responsible investigator, c) The relocation or closure of the sites where the study or research will be conducted, or the addition of new sites,

ç) A change in the cosmetic products or raw materials on which the study or research is based, d) A change in the name/trade name of the cosmetic products or raw materials on which the study or research is based, e) A change in the manufacturer of the cosmetic products or raw materials on which the study or research is based, f) Changes in the information related to the manufacturing of the cosmetic products or raw materials on which the study or research is based, g) A change in the duration and frequency of use of the cosmetic products or raw materials on

Unofficial English translation for information purposes only. In the event of any discrepancy, the Turkish original text (mevzuat.gov.tr) shall prevail.

which the study or research is based, ğ) The replacement of cosmetic products or raw materials used for comparison purposes in the study or research, if any, h) Changes in the critical characteristics of the cosmetic products or raw materials on which the study or research is based; changes in their stability, structure, effect, formulation and the like, ı) A change in the safety assessments of the cosmetic products or raw materials on which the study or research is based, i) A change regarding the safety of the cosmetic products or raw materials on which the study or research is based, during their application to volunteers, j) A change in the scientific value of the study or research, k) Changes in the manner or method of conducting the study or research, l) Amendments to the study or research protocol, m) A change in the purpose of the study or research, n) A change in the design of the study or research, o) A change in the ICF, ö) A change in the method of recruiting volunteers for the study or research, p) The addition or removal of tests or measurements, or changes in their methods, r) A change in the number of volunteers, s) A change in the age range of the volunteers, ş) A change in the inclusion and exclusion criteria of volunteers for the study or research, t) A change in the statistical analysis method. (4) An application regarding an amendment shall contain at least the following information:

a) A sample application cover letter appropriate to the subject, b) The current application form published on the Agency's website; 1) The full title of the study or research, and the protocol code number, if available, 2) The sponsor, the contract research organization to be assigned by the sponsor, or the responsible investigator, 3) The version number and date of the updated amendment, 4) Indication of the amendments by underlining, and, if possible, a summary of the amended documents, 5) The probable consequences for the volunteers included in the study or research and the evaluation of these consequences. (5) Authorization from the Agency is not required for amendments other than significant amendments. However, the Agency shall be notified of such amendments. Suspension of studies or research

ARTICLE 8- (1) If, during the conduct of a study or research, the Agency determines that one of the existing conditions under which it authorized the study or research has ceased to exist, it shall immediately suspend the study or research. If these conditions are not fulfilled within the period granted by the Agency, or if it is understood that they cannot be fulfilled, or if the health of volunteers is put at risk within this period, the study or research shall be terminated directly. (2) In cases that do not involve an evident risk for the volunteers, the opinions of the sponsor, the contract research organization to be assigned by the sponsor, or the responsible investigator on the matter may be requested, and in such case, the opinions on the matter must be submitted to the Agency within fifteen working days. Notification of the termination of studies or research

ARTICLE 9- (1) The sponsor, the contract research organization appointed by the sponsor, or the principal investigator shall notify the relevant ethics committee and the Agency of the termination of the study or trial within ninety days of the date of such termination. (2) Where the study or trial has not been initiated on the date specified in the application dossier despite having been authorized by the Agency, the reasons for non-initiation shall be notified to the Agency within ninety days; the start date may, where necessary, be postponed by the Agency. (3) The study or trial protocol shall include a section on the termination of the study or trial. The date of the last visit of the last participant (volunteer) included in the study or trial may be specified as the termination of the study or trial. Any exceptional case shall be set out in the protocol together with its justification. (4) The sponsor, the contract research organization appointed by the sponsor, or the principal investigator shall inform the Agency in cases where the study or trial is not initiated after authorization has been obtained from the Agency, or is not re-initiated after having been suspended. This notification shall include a brief written statement explaining the reasons for not initiating and for terminating the study or trial. (5) The sponsor, the contract research organization appointed by the sponsor, or the principal investigator shall submit the final report of the study or trial to the Agency within ninety days of the termination of the study or trial. Entry into Force

ARTICLE 10- (1) This Guideline shall enter into force upon the approval of the President of the Agency. Execution

Unofficial English translation for information purposes only. In the event of any discrepancy, the Turkish original text (mevzuat.gov.tr) shall prevail.

ARTICLE 11- (1) The provisions of this Guideline shall be executed by the President of the Agency.

REVISION HISTORY Revision No Revision Date Justification and Explanations 1 15.11.2022 An update has been made regarding systemic requirements.

Unofficial English translation for information purposes only. In the event of any discrepancy, the Turkish original text (mevzuat.gov.tr) shall prevail.