GUIDELINE ON ARCHIVING PRINCIPLES IN CLINICAL TRIALS 13 NOVEMBER 2015

1. PURPOSE The purpose of this guideline is to clarify the methods to be followed in order to ensure that the archival material of clinical trials held by the coordinator, administrative responsible person, principal investigator, sponsor or contract research organization is not lost for any reason, that it is protected under the required conditions, and with respect to the screening out and destruction of material that is not deemed necessary to retain. The guideline provides guidance on the retention of documents related to clinical trials and explains the details of the application of the applicable relevant legislation. 2. DEFINITIONS The definitions set forth in the Guideline for Good Clinical Practice and in the relevant legislation shall apply. Other definitions not included therein are as follows: 2.1. Archive: The documentation retained in accordance with the legislation related to clinical trials, or the premises housing such documentation. 2.2. Archival Material: Materials containing all kinds of files and documentation that must be retained after the completion of the trial in accordance with the legislation related to clinical trials. 2.3. File: A group of documents pertaining to the same subject. 2.4. Filing: The process of recording all documents generated, processing them, and retaining them in a certain order for future reference when necessary once the work is completed. 3. RESPONSIBILITY FOR PROTECTION 3.1. The coordinator, administrative responsible person, principal investigator, sponsor or contract research organization is responsible for protecting the clinical trial documentation and archival material in their possession from all kinds of harmful effects and elements, and for classifying and retaining them in their original order. 3.2. The coordinator, administrative responsible person, principal investigator, sponsor or contract research organization shall ensure the following with respect to the protection of archival material: 3.2.1. Shall take the necessary measures against fire, theft, humidity, flooding, dust, and all kinds of damage by animals and pests, 3.2.2. Shall keep fire extinguishers permanently operational in accordance with fire instructions to protect against fire, 3.2.3. Shall maintain the humidity between 50-60% by placing hygrometers in appropriate locations in every section of the archive, 3.2.4. Shall use moisture-absorbing devices or chemical substances to prevent excess humidity, 3.2.5. Shall disinfect archive depots at least once a year as a protective measure against microorganisms, 3.2.6. Shall arrange the lighting and ventilation systems in a suitable manner, 3.2.7. The temperature shall be kept constant as far as possible. 4. CONFIDENTIALITY OF ARCHIVAL MATERIAL 4.1. Archival material held by the coordinator, administrative responsible person, principal investigator, sponsor or contract research organization that is deemed confidential during the period in which the trial is ongoing shall remain confidential after being transferred to the archive. 4.2. Measures shall be taken to ensure that the archive can be accessed only by authorized persons and that access is restricted to persons other than these. 5. USE OF ARCHIVAL AREAS OUTSIDE THE INSTITUTION OR ORGANIZATION 5.1. In cases where sufficient areas for archiving are not available at the institution where the trial is conducted or at the sponsor or contract research organization, support may be obtained from a domestic archiving company deemed suitable by the Turkish Medicines and Medical Devices Agency, located outside the institution or organization.

5.2. In cases where external archiving support is obtained, permission for transfer shall be obtained by submitting the situation together with its justifications to the Turkish Medicines and Medical Devices Agency. 5.3. The coordinator, administrative responsible person, principal investigator, sponsor or contract research organization shall verify that the conditions specified in this guideline are also met in the area to be provided by the archiving company. 5.4. There shall be no facilities in the vicinity of the facility where external archiving support is obtained such as industrial, chemical storage facilities, paint or plastic factories, fuel filling and storage facilities, and heavy industry facilities that have explosive or flammable properties. 5.5. All systems at the facility where external archiving support is obtained shall be subject to periodic maintenance and controls and shall be kept ready for submission upon request. 5.6. In cases where more than one sponsor or contract research organization receives services from the same archive unit, they shall

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separately meet the requirements set forth in this guideline, the documents of each company shall be archived in separate sections in a manner that prevents them from being mixed with one another, and the principle of confidentiality shall be complied with. 5.7. When the retention period specified in the relevant legislation expires, the archival materials may be sent abroad, provided that the relevant parties are informed and the principle of confidentiality is complied with. 5.8. If the sponsor has a validated electronic archive system capable of presenting the originals of the archival materials upon request by the relevant authority, it may send abroad financial disclosure documents, investigator curricula vitae whose originals have been submitted to the Agency, protocol/protocol amendment signature pages, confidentiality documents and monitor monitoring reports even before the retention period specified in the relevant legislation expires. 6. PREPARATION AND SUBMISSION OF ARCHIVAL MATERIAL 6.1. After the completion of clinical trials, all documentation is reviewed. The essential documents that the coordinator, administrative responsible person, principal investigator, sponsor or contract research organization is required to hold in its possession in accordance with the relevant legislation are separated. 6.2. The material to be sent to the archive is submitted after being recorded on the archive registration form. 6.3. The sponsor or contract research organization shall have determined the filing and archiving methods by means of a standard operating method in compliance with the relevant legislation. 6.4. An archiving responsible person shall be present within the structure of the sponsor or contract research organization, and all archive records shall be kept in a specific location. 7. RETRIEVAL OF MATERIAL FROM THE ARCHIVE 7.1. The sponsor or contract research organization shall have determined the method for how material will be retrieved from the archive. Material sent to the archive may need to be retrieved for inventory checks, audits or other reasons. 8. DESTRUCTION OF ARCHIVAL MATERIAL 8.1. Upon the expiry of the archiving period of the documents pertaining to the clinical trial, the sponsor informs the coordinator, the administrative responsible person, the principal investigator and the archiving responsible person in writing that the documents are to be destroyed. 9. APPLICATION AND PERMISSION 9.1. The required permission is granted by the Turkish Medicines and Medical Devices Agency to institutions or organizations wishing to operate for the purpose of retaining documents related to clinical trials. 9.2. Institutions or organizations wishing to obtain permission shall make an application to the Turkish Medicines and Medical Devices Agency with the relevant application form by paying the application fee specified on the website of the Turkish Medicines and Medical Devices Agency.

9.3. Institutions or organizations whose applications are deemed suitable shall have their inspection carried out within 45 (forty-five) days at the latest. After the permission granted by the Turkish Medicines and Medical Devices Agency, an inspection shall be carried out at least once a year. 10. REPEALED PROVISIONS The "Guideline on Archiving Principles in Clinical Trials", which was put into effect by the Approval of the Authority dated 06.08.2014 and numbered 95052, has been repealed. 11. ENTRY INTO FORCE This guideline enters into force on the date of its approval. Dates and Numbers of the Publication of Amendments Made to the Guideline Date Number 1. 28.01.2011 843 2. 06.12.2011 10990 3. 23.08.2011 7481 4. 17.04.2013 43020 5. 06.08.2014 95052

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