Administrative Notice
June 5, 2024

To: Prefectural Health Department (Bureau)

Medical Device Evaluation Division,
Pharmaceutical Safety Bureau,
Ministry of Health, Labour and Welfare

Examples of Points to Consider and Approaches for Utilization of Study Results Obtained from Specified Clinical Research in Applications for Approval of Medical Devices and Regenerative Medical Products

As one of the supplementary resolutions for the establishment of the Clinical Trials Act (Act No. 16 of 2017), it is stipulated that “clinical research should be promoted by clarifying regulatory classifications of clinical trials and clinical research and how they can be utilized, and a mechanism that enables the utilization of information obtained from clinical research for application materials for approval of drugs, medical devices, etc. should be considered promptly to promote the development of pharmaceuticals, medical devices, etc.” In relation to this, the points to consider and approaches for pharmaceuticals are presented in “Examples of Points to Consider and Approaches for Utilization of Study Results Obtained from Specified Clinical Research in Applications for Approval of Pharmaceutical Products” (administrative notice of the Pharmaceutical Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labour and Welfare, dated March 31, 2023; hereinafter referred to as “Administrative Notice on Pharmaceutical Products”).

On this occasion, it was commented in "Project for Examination of the Data Reliability, etc. for the Regulatory Approval of Software as Medical Device” (Representative: Nakano Shohei, Executive Director, Japan Association for the Advancement of Medical Equipment) that while results from confirmatory trials are required for applications for approval in principle, whether the information obtained from specified clinical research of medical devices (including software as medical device (SaMD), same applies hereinafter) can be utilized for regulatory purpose needs to be determined individually

considering such as whether the medical device can be evaluated with the study results obtained, status of retention of supporting records/documents, and difficulty in conducting and reproducing clinical trials, etc.

Considering the above, examples of points to consider and approaches for utilization of study results obtained from specified clinical research, including those for regenerative medical products, are presented in the Appendix with consideration of the Administrative Notice on Pharmaceutical Products. Please fully inform this to the related business operators under your administration.

It should also be noted that this administrative notice provides examples based on individual cases of regulatory applications and does not necessarily apply to all cases of regulatory applications, and will be subject to review with future consideration, accumulation of knowledge, etc.

In addition, please be noted that a copy of this administrative notice will be sent to the organizations, etc. listed in the Separate Note.

Appendix

Examples of Points to Consider and Approaches for Utilization of Study Results Obtained from Specified Clinical Research in Applications for Approval of Medical Devices and Regenerative Medical Products

1. Whether specified clinical research can be utilized as application materials for approval shall be determined comprehensively in consideration of the examples of considerations and concepts for ensuring reliability shown in 2 below, as well as the background information such as the status of the conduct of specified clinical research, the status of publication of study results obtained from the specified clinical research, and the status of descriptions in the related guidelines, etc. PMDA should be consulted at an early stage if the study results obtained from the specified clinical research are being considered for use in the applications for approval.

2. If study results obtained from specified clinical research are being used for applications for approval, the level of reliability required will be determined with comprehensive consideration of the significance, etc. of the clinical research in the applications for approval. The investigator of the specified clinical research should ensure the appropriate conduct of the clinical research, including retention of supporting records/documents, and should be able to explain the status of ensuring reliability of the research.

   Please note that whether the study results of specified clinical research being used for applications for approval meet the required level of reliability will be confirmed by document-based inspection after the application is submitted for approval, except in the case of applications for approval based on “Handling of Off-label Use of Medical Devices for Healthcare Professionals” (joint notification by the Director of Research and Development Division, Health Policy Bureau and the Director of the Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare, dated May 22, 2006).

   In addition, whether the confirmation of supporting records/documents at the medical institution which conducted the specified clinical research is necessary will be determined based on the required level of reliability and the results of document-based inspection for the applicant or the investigator of the specified clinical research. For this reason, it is desirable that the applicant establishes a cooperative operation with the investigator for the compliance inspection.

   The followings are the specific examples of considerations and concepts to fulfill the required level of reliability based on individual application cases:

(1) The investigator of the specified clinical research should be able to appropriately explain the appropriateness of the process of the preparation of dataset from case report form, analysis, and the preparation of clinical study report as well as the reliability of data. Also, the applicant should be able to confirm appropriateness of such procedure and reliability of data in using the study results obtained from the specified clinical research for applications for marketing approval of medical devices and regenerative medical products.

(2) The investigator of the specified clinical research should be able to appropriately explain that storage, etc. of the medical devices and regenerative medical products used in the specified clinical research are conducted adequately.

(3) Regarding the monitoring method, on-site monitoring, combination of on-site monitoring and central monitoring, or central monitoring may be selected depending on the risk and feasibility; however, in any case, the investigator of the specified clinical research should be able to appropriately explain the validity of selecting the specific monitoring method.

(4) The necessity and method of audit may be decided according to the risk and feasibility; however, in any case, the investigator of the specified clinical research should be able to appropriately explain the validity of selecting the specific audit method.

(5) Review of source records by direct access in monitoring and audits does not necessarily need to cover all subjects; however, the investigator of the specified clinical research should be able to appropriately explain the validity of the subjects, items, etc. extracted for direct access according to the risks and feasibility.

(6) If an audit is conducted, the investigator of the specified clinical research should be able to appropriately explain that the audit was conducted by a third party independent from the specified clinical research being audited (e.g., audit is conducted by the research support department, etc. of the Clinical Research Core Hospital for which independence from the specified clinical research can be confirmed).

(7) The investigator of the specified clinical research should be able to appropriately explain the status of collection of information and its validity on malfunctions, etc. related to medical devices and regenerative medical products used in the specified clinical research from the viewpoint of the protection of research subjects.

3. If the data obtained from the specified clinical research are used for the applications for approval, the investigator of the specified clinical research should obtain appropriate patient consent to allow the use of the study data by the applicant.

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Separate Note

The Japan Federation of Medical Devices Associations
American Medical Devices and Diagnostics Manufacturers' Association
European Business Council Medical Equipment and IVD Committee
Japan Pharmaceutical Manufacturers Association (JPMA)
The Japan Digital Health Alliance
Japan Medical Venture Association
Council for AI Medical Devices
Forum for Innovative Regenerative Medicine
Japan Medical Association
The Japanese Association of Medical Sciences
Japan Dental Association
Japanese Society of Hospital Pharmacists
Japan Nursing Association
Japan CRO Association
Japan Association of Site Management Organizations
Pharmaceuticals and Medical Devices Agency
Regional Bureaus of Health and Welfare