

**GCP Compliance Review**  
**Notification No. 0715006 issued July 15, 2005**

The Japanese Ministry of Health, Labor and Welfare (MHLW) has issued Notification No. 0715006 in July 2005 as additional information to the new Good Clinical Practice (GCP) regulation effective from April 1, 2005. This regulation covers GCP compliance reviews of clinical trial documentation for medical device *shonin* applications. The reference documentation will be attached to the MAH *shonin* application dossier and will review all reference documentation related to the clinical trials. The Pharmaceuticals and Medical Devices Agency (PMDA) and the MHLW will conduct the review to confirm that the clinical trials have been conducted in accordance with the Japanese GCP. This regulation is based on the following laws:

- Pharmaceutical Affairs Law article 14 clause 5, 19-2 clause 5
- Enforcement Ordinance of the Pharmaceutical Affairs Laws article 27, 43
- Enforcement Regulation of the Pharmaceutical Affairs Law article 42 clause 2

1. **Reference documentation for GCP compliance review:**

- a. The reference documentation to be reviewed will be all clinical trial documentation. However, clinical trial documents that have been already submitted in a previous *shonin* application dossier, or documents that are part of a dossier that has already received *shonin* approval, are ***exempt*** from the review process.
- b. The following documents should be included in the clinical trials documentation:
  - i. Clinical trial protocol and other related documentation.
  - ii. Selection process of the clinical trial organization.
  - iii. Information on the company that requests the clinical trial (referred to as the primary investigator) and contract between the primary investigator and research institution of the clinical trial.
  - iv. Monitoring report.
  - v. Adverse effect report.
  - vi. Case report.
  - vii. Data collection and analysis report.
  - viii. Clinical trial final report.
  - ix. Information on the management, maintenance, and storage of the clinical trial devices.
  - x. Clinical trial summary report.

2. **Organizations conducting GCP compliance review:**

- a. The PMDA will review the reference documentation when the *shonin* application is submitted to the PMDA.
- b. The MHLW will review the reference documentation when:
  - i. The PMDA cannot review the documentation because of such reasons as the reference documentation cannot be delivered to the PMDA office successfully.

- ii. The Officer of Pharmaceutical and Medical Safety Bureau of the MHLW questions the credibility of the documentation.

3. **Medical device GCP site audit:**

The PMDA needs to verify that a primary investigator (such as a medical device company or physician) generated the clinical data for new devices or partial change applications in accordance with Japanese Medical Device GCP. This inspection will be done by submission of documentation **AND/OR** by a site audit.

a. Those who will be audited:

- i. Those who **request clinical trials that generate the clinical data** for the *shonin* applications, such as a primary investigator. Primary investigators include device companies, physicians, or CROs.
- ii. Those who actually **conduct the entire or partial clinical trials (with or without a request) that generate the clinical data** for the *shonin* applications, such as the Director of Investigational Site, which includes physicians at hospitals.
- iii. If the trials are cancelled or temporarily stopped, the primary investigator and/or investigational site will be checked by the PMDA.

b. Conditions for a site audit.

Based on the results of the documentation review, either the MHLW or the PMDA will determine whether or not a site audit is necessary.

c. Who conducts the site audit.

A site audit will review the research institution and related office buildings. If the GCP inspection application has been already filed to the PMDA, the PMDA officials will conduct the site audit. If the MHLW believes a site audit is necessary, the MHLW officials will conduct the site audit.

d. Site audit procedure.

When the MHLW decides the site audit is necessary, the MHLW will notify the company that requested the clinical trials (above a(i), primary investigator) and/or notify the company that actually conducted the clinical trials (above b(ii), physicians) before visiting the site.

e. GCP Site Audit.

For the company that requested the clinical trials → it is necessary to confirm the trials were conducted in accordance with the Japanese Medical Device GCP Ordinance Chapter 2, section 1 and Chapter 3, section 2.

For the company that actually conducted the clinical trials → it is necessary to confirm the trials were conducted in accordance with the Japanese Medical Device GCP Ordinance Chapter 2, section 2 and Chapter 3, section 2.

For the company who conducted the clinical trials based on a request → it is necessary to confirm the trials were conducted in accordance with the