

GCP Division, Activity Summary of the 12th Term (April 2014 – March 2016)	
Study Group	Study Group 1: QMS
Subgroup	C-1-A
Theme	Construction of a Quality Assurance System for Clinical Trials
<p>Subgroup A, Study Group 1 (hereinafter, this group) worked on the following tasks based on the Clinical Trial Quality Assurance (CTQA) Model proposed in the deliverable “Toward the Construction of a Guideline for Quality Assurance for Clinical Trials – Proposal of a Clinical Trial Quality Assurance (CTQA) Model – Assuring the quality of clinical trials” (Document No. 13C015) produced by Subgroup C, Study Group 2 in the previous term. This group deepened our insights regarding the quality assurance of clinical trials, and considered the creation of an updated CTQA model as well as methods for its utilization.</p> <p>To update the CTQA model, this group focused on the monitoring process out of clinical trial processes, and further divided the monitoring process into “monitoring (activities by the sponsor)” and “activities by the clinical trial site” to investigate matters such as objective indices (metrics) for assuring the quality of the process.</p> <p>In the deliverable of the present term, we updated the CTQA model with a focus on conduct of clinical trial (activities by the clinical trial site) and monitoring (activities by the sponsor). This group purpose was to create a document which would serve as a guide for quality assurance of various processes in clinical trials, and as a practical reference manual for personnel ranging from inexperienced monitors to monitor leaders.</p> <p>The tables were also refined to display input, resources, systems, output, risks, metrics, conditions, etc. for each clinical trial phase and task process, and to make it easier to visualize, in concrete terms, the process of extracting metrics from input and output information.</p> <p>ICH-E6 (R2) is due to be released as a final version (Step 4) in November 2016. Such realities pertaining to GCP indicate that quality assurance in clinical trials will be required to make a shift from focusing on output quality control to process control as a matter of necessity. The CTQA model was proposed as a practical tool for quality assurance in clinical trials to shift to process control.</p> <p>Using the CTQA model helps to clarify the verification activities and metrics for quality assurance in clinical trial processes. Hence it may become possible to make specific proposals in, for example, risk-based monitoring.</p>	

The use of the CTQA model also holds promise for easier identification of opportunities for improvement by enabling the clarification of metrics and KPIs in the implementation of Corrective and Preventive Actions (CAPAs) incorporated into ICH-E6 (R2). For example, each company can set appropriate measurement times and target values or evaluation criteria for the established metrics before performing verification activities, and then monitor the measurements and state of the metrics, performing CAPAs as necessary if the measurements or state of the metrics are not desirable.

GCP Division, Activity Summary of the 12th Term (April 2014 – March 2016)	
Study Group	Study Group 1: QMS
Subgroup	C-1-B
Theme	Construction of Clinical Trial of Quality Assurance Systems Expected of CROs: A Deliberation of Real Quality Assurance Systems to Meet Client (Manufacturer) Requirements
<p>In regard to issues which arise from the sponsor and contract research organization (CRO) working together in contracted business, the Japan CRO Association and the Japan Pharmaceutical Manufacturers Association (JPMA) have made proposals regarding matters which call for future action.</p> <p>In this context of rising interest in the contracted business relationship of sponsor and CRO, our group addressed the theme, “The Construction of Clinical Trial of Quality Assurance Systems Expected of CROs.”</p> <p>In the process of our deliberations, we felt that if we could identify and present discrepancies between sponsor and CRO in relation to contracted business services, it would serve as extremely meaningful information in helping to make contracted business services proceed smoothly.</p> <p>Therefore, to detect such discrepancies, we conducted questionnaire surveys of both the sponsor and CRO to compare the results from each.</p> <p>The results allowed us to detect and present several matters which appeared to be discrepancies between the sponsor and CRO.</p> <p>For the sponsor and CRO to have knowledge and understanding of such discrepancies is likely to be an aid to mutual understanding.</p> <p>Through such understanding, the sponsor and CRO can work together more cohesively, which will ultimately lead to the benefit of patients who await new drugs.</p> <p>We hope the activities of our group this term will be an aid to that process.</p>	

GCP Division, Activity Summary of the 12th Term (April 2014 – March 2016)	
Study Group	Study Group 1: QMS
Subgroup	C-1-C
Theme	A Proposal for the Establishment of Practical QMS in Clinical Trials – as Guidance for the Introduction and Establishment of QMS in the Front Lines of Clinical Trials –
<p>Conventionally, it was generally understood that the quality of clinical studies, in particular clinical trials, was to be maintained and assured by careful monitoring and quality control of all sites. However, in recent years, the concept of a quality management system (QMS) which assures quality through systematic and organizational methods is becoming mainstream. The current situation is one in which most clinical trial sponsors, CROs, and SMOs possess the necessary functions to implement clinical trial operations; yet, it is debatable whether the systems and means in place are appropriate as a QMS. In the present term, we attempted to create a “Guidance for the Introduction of QMS” which makes it possible to construct a practical QMS by each of the companies considering the introduction of QMS to coordinate their existing mechanisms and identify the functions which do not exist. We therefore divided QMS introduction into two perspectives, that is, the study level perspective in which the QMS is constructed and operated from the standpoint of correcting and/or preventing issues which may arise in the respective clinical studies, and the perspective of clinical trial implementation systems and planning, including SOP/educational systems and study team composition methods. With these two perspectives as subthemes, our members were grouped into teams based on their objective for participation.</p> <p>Team A investigated the introduction of QMS in relation to events during monitoring. When constructing a QMS at the clinical study level, the important objects of quality management are the events which occur during monitoring. Out of these events, the team considered “timing of monitoring,” “target sample size,” “(first time) IRB validity,” “obtainment of informed consent,” “deviations,” and “SAE reports/action” to be of particular importance. The team raised the critical quality management issues as specific cases in these events, and discussed their control and risk management, that is, which departments might use which indices for measurement and evaluation to implement the PDCA cycle so that cases could be prevented from recurring or occurring. Through these discussions, the team came to believe that in each case of the events, the QMS can be systematized by reorganizing the existing functions and/or sections at each company. Meanwhile, to implement the PDCA cycle effectively, the team thought that, in addition to constructing the system, it was important to set and control quality targets and evaluation indices appropriately.</p>	

Team B investigated the “Introduction of a Proactive QMS” which leads to continuous improvement of the clinical trial implementation system and planning. In the process, the team identified the incorporation of a “CAPA management system” to be a key point which would lead to such continuous improvement, and deliberated on “process models for CAPA management” and “specific examples of CAPA management for noncompliance issues” with the goal of producing deliverables which each company could use to introduce a “CAPA management system.”

In “process models for CAPA management,” the team set up a QM function responsible for cross-functional quality management, and established the flow and timeline for the CAPA management process. In addition, the team identified the lead (responsible person), relevant parties, authorizer, and the specific actions required in each of the processes of “detection, reporting, and control of noncompliant events,” “emergency/remedial correction of noncompliance,” “assessment of noncompliance levels,” “root cause analysis,” and “CAPA plan, implementation, effectiveness check,” keeping in mind the differences between clinical trial specific issues and systematic issues shared across multiple clinical trials.

In “specific examples of CAPA management for noncompliance issues,” the team performed modeling of “GCP noncompliance notification and assessment form” and “CAPA management form.” Using four specific examples, the team examined the implementability of the “process model for CAPA management.”

GCP Division, Activity Summary of the 12th Term (April 2014 – March 2016)	
Study Group	Study Group 1: QMS
Subgroup	C-1-D
Theme	Risk Management Relating to Clinical Trials for Medical Devices
<p>JSQA Medical Devices Subgroup (C-1-D) looked into the differences unique to clinical trials for medical devices within the issue of QC/QA in medical device clinical trials to date. Through our examinations, we identified characteristics unique to medical devices which differ from the development of pharmaceuticals.</p> <p>Such characteristics of medical devices include sequential modifications and/or small improvements on a regular basis. However, clinical trials are not necessarily attached to all application documents and the number of medical device clinical trials implemented in Japan is extremely smaller than pharmaceuticals, due to the market size of medical devices and cost-effectiveness to conduct the clinical studies in medical devices.</p> <p>For these reasons, many corporations have less experience with clinical trials for medical devices than pharmaceuticals. Therefore, in past Special Projects for Medical Devices, the special requirements from QA/QC perspectives during planning phase of clinical trials, as well as the special characteristics of clinical trials for medical devices, had been examined. In the last term, we mainly considered the issues which have the potential of becoming critical problems in implementing the clinical trial in terms of risk.</p> <p>This term, we prepared a summary in the form of explanatory documents, building on the work of the previous session to share information on risk management and make it generally known. When performing risk management, we believe it is necessary for the organization (company) to work in advance to determine the gravity and frequency of risks and define their risk tolerance range, and to form teams of several people to discuss and assess how to evaluate the risks which may occur in clinical trials. For that end, it is necessary for members implementing those tasks to share a basic understanding. Hence we aimed to formulate explanatory documents to clarify that understanding.</p> <p>This document shows the outline of risk management. We could not prepare the tools for performing risk management, but we feel our deliberations were a success in that we were able to demonstrate one way of thinking.</p> <p>Through our activity, our members are aware that risk control, assessment, and management are necessary in every aspect of clinical development, not limited to the development of medical devices. We feel there is a need to continue acting on the basis of risk management even after our deliberations have ended.</p>	

1

GCP Division, Activity Summary of the 12th Term (April 2014 – March 2016)	
Study Group	Study Group2: Audit
Subgroup	C-2-A
Theme	Aiming at Effective and Efficient GCP Auditing by Introducing the Concept of ICH Q8 and Q9 – Significance of Introduction, and Proposal for Actual Introduction Part 2
<p>Purpose</p> <p>With the aim of making a proposal that would transcend boundaries of the region, sponsor, or clinical trial site to harmonize the basic concepts and specific methods for effective and efficient implementation of audits which are performed as a part of quality assurance in international joint clinical trials, we studied the concepts of “ICH guidance Q8: Pharmaceutical Development” and “ICH guidance Q9: Quality Risk Management” which pertain to quality in the manufacture of pharmaceuticals and are included in the guidelines issued by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). We investigated whether the concepts are applicable to audits for each of the processes in clinical trials in Japan.</p> <p>Method</p> <ol style="list-style-type: none"> 1. We divided the “<u>clinical trial processes</u>” into several processes. 2. We divided each of the processes into several sub-processes. 3. On the basis of cases, we identified the harms in each sub-process, the process parameters (PP), and the details of PP deviations. 4. We identified the critical process parameters (CPP) of each sub-process. 5. We pinpointed the conceivable causes and also identified conceivable measures for prevention and elimination. <p>In this fiscal year, we examined the processes of “<u>examination, observation, and evaluation.</u>”</p> <p>Results</p> <p>It became clear that there was “localization” in the matters pointed out in the GCP compliance investigation (harm), the PP, and the details of PP deviations in the most recent 4 years from 2008 to 2012.</p> <p>The CPP for the inspection process, which is one of the subprocesses of “inspection, observation, evaluation,” was “frequency of inspections.”</p> <p>Conclusion</p> <p>It was suggested that, in audits of “examination, observation, and evaluation” out of the</p>	

processes of clinical trials in Japan, a focus on specific parameters would make it possible to perform continuous improvement and maintenance of the quality assurance system through effective and efficient evaluation of said quality system and by the proposal of appropriate preventative and corrective actions based on said evaluation results.

GCP Division, Activity Summary of the 12th Term (April 2014 – March 2016)	
Study Group	Study Group 2: Audit
Subgroup	C-2-B
Theme	An Investigation of Auditing Techniques in Clinical Trials with a Risk-based Approach to Quality Management
<p>Subgroup B, Study Group 2 (“our group”) deliberated on the issue of “auditing techniques in clinical trials with a risk-based approach to quality management.”</p> <p>In past study group sessions of JSQA, numerous discussions were held on various themes in regard to this issue, including “basic concepts in risk-based quality management” in clinical trials, “methods for analysis and detection of harm and hazards,” and “scoring the importance of harms and hazards and comparing them from a QC/QA perspective.”</p> <p>However, we believe the discussions had not reached the point of determining whether, when analyzing and evaluating these injuries and/or hazards inherent in clinical trials, and performing risk-based quality management of the clinical trial, there is a need for change in the “timing, objects, and methods of audit” and “methods for evaluation of audit observation results found by the audit” of conventional auditing techniques, and if there is a need for change, what matters require consideration.</p> <p>In future, we believe the quality management of clinical trial operations will require a review of the conventional auditing techniques which involve retrospective verification, such as “exit surveys” and “retrospective audit (retrospective QA),” given that the quality management of clinical trial operations will incorporate a risk-based approach following the issuance of the office memorandum “Basic approach relating to risk-based monitoring (July 2013)” from Japanese authorities, the USFDA “Oversight of Clinical Investigations -A Risk-Based Approach to Monitoring,” and the EMA “Reflection paper on risk based quality management in clinical trials,” as well as the addendum to ICH E6: Standard guidelines relating to implementation of clinical trials for pharmaceuticals (draft, November 16, 2015).</p> <p>Therefore, our group conducted study sessions on risk-based monitoring over the course of approximately one year, through which members acquired knowledge on risk-based monitoring and discussed definitions. The following three subtitles were set up to investigate our issue.</p> <ol style="list-style-type: none"> 1. A questionnaire survey to determine the “status of introduction of risk-based monitoring and risk-based auditing in each company involved in Japanese clinical trials” <ul style="list-style-type: none"> ➤ Questionnaires were distributed to 186 corporate members of the GCP Division, out of which 102 companies responded. The questionnaire responses included 15 companies 	

indicating they “had introduced central monitoring as risk-based monitoring” and 11 companies saying they “had scoring systems for risk assessment on which to formulate the audit plan.” On the other hand, there were also comments such as, “we have no data to use for a scoring system” and “we do not see the significance of a scoring system, as the results of all conceivable factors should be deliberated.”

2. Investigation of how the audit might be affected by the introduction of risk-based monitoring into clinical trials
 - We set up specific clinical trial models and discussed the effects of the introduction of risk-based monitoring on the on-site audit. Additionally, we discussed how the “monitoring plan” and “central monitoring,” which rise in importance may affect the audit.
3. Investigation of auditing techniques which incorporate risk-based approach
 - We identified risks and performed risk analyses in regard to deviations and audit findings contributed by our group members. The results were compiled and conducted risk assessment and trend analysis. Through this process, we validated the types and timing of audits and deliberated measures for risk reduction.

In conclusion, we hope our investigations will be an aid to reviewing auditing techniques. We also feel there is a need for continued deliberation on this issue.

GCP Division, Activity Summary of the 12th Term (April 2014 – March 2016)	
Study Group	Study Group 2: Audit
Subgroup	C-2-C
Theme	Preparation of a “Q&A for GCP Quality Management and Quality Assurance Managers”
<p>It appears that reading through the GCP ministerial ordinance, guidance, and notifications does not necessarily yield clear information on how to deal with specific situations encountered in clinical trials. We felt that investigating specific cases might also be an aid to understanding the GCP ministerial ordinance, guidances, and notifications</p> <p>In the previous (11th) term, Special Project Group 9 of the GCP Division looked into commonly encountered cases of audit findings and produced the deliverable, “Q&A for Audit Findings (Examples),” as material to be used by the GCP Division. Subgroup C-2-C continued the Special Project Group 9’s activities of the previous term, collecting and reviewing issues from commonly encountered cases while avoiding redundancy with other Q&As, and formulating answers. As in the previous term, the deliverable will be summarized into Q&A form and uploaded to the JSQA member website as “Q&A for GCP Quality Management and Quality Assurance Managers,” together with the cases prepared in the previous term by Special Project Group 9. For better convenience when searching for relevant cases, the Q&A compilation will feature a listing categorized by GCP provisions, plus an added search function.</p>	

GCP Division, Activity Summary of the 12th Term (April 2014 – March 2016)	
Study Group	Study Group 3: Electronic
Subgroup	C-3-A
Theme	An Investigation of Clinical Trial Operations Utilizing Computerized Systems
<p>Team 1</p> <p>Working under the theme, “survey on changes in the EDC environment,” Team 1 of Subgroup A conducted a web questionnaire survey of pharmaceutical company members of the JSQA GCP Division, member companies of the Japan CRO Association (JCROA), and member companies of the Japan Association of Site Management Organizations (JASMO), from April to July 2015, to compare the results with those of questionnaire surveys conducted in Terms 9 and 10. The team compared and analyzed the results, and extracted issues requiring attention regarding the use of EDC systems.</p> <p>From the survey aimed at pharmaceutical company members of the JSQA GCP Division, it was found that the use of EDC was significantly more frequent compared to the time of the Term 9 survey, indicating there had been a change in the usage situation. Overall satisfaction in EDC was significantly higher. New issues included the need for foreign language services in international joint clinical trials and help desks, sponsor dissatisfaction in regard to cost, and lack of human resources for EDC construction and operation.</p> <p>In the questionnaire survey of JCROA member companies, the items which many respondents considered “problematic and low in satisfaction” were “system response speed and stability,” “user training/manual,” “system operability,” and “use of English.” These problems faced by CROs are also likely to be important issues for pharmaceutical companies.</p> <p>The questionnaire responses by JASMO member companies indicated more widespread use of EDC compared to the results of the Term 10 questionnaire. Other issues identified included “issues relating to waiving of EDC training,” “changes in the installation and utilization of the help desk,” “issues accompanying EDC lock-out,” “reduction of SDV frequency,” “issues relating to setting of queries,” and “issues of CRF (copy) storage.”</p> <p>Team 2</p> <p>Now that it is mandatory to submit clinical data in CDISC compliant electronic form when filing applications for approval, Team 2 of Subgroup A worked under the theme, “quality assurance activities in the context of CDISC standardization” to investigate the key points for ensuring quality at each stage of CDISC compliance operations.</p> <p>The electronic data required when filing applications for approval must be in a format compliant with CDISC standards. Noncompliant data is not permitted. Therefore, from the planning stage of the clinical trial, it is desirable to keep in mind that the submission of data</p>	

compliant with various standards will be required at the time of application, and to consider data collection and analysis procedures accordingly. In addition, documents to be submitted consist not only of SDTM and ADaM datasets but also of the data definition document and other accompanying documentation. Therefore, there is a need to organize in-house procedural manuals and implement procedures for each of the documents to be submitted.

Keeping these matters in mind, we investigated documents relating to the preparation of SDTM and ADaM datasets as well as the QC/QA systems for those documents, and identified tools which can be utilized according to preparation procedures, methods for quality management, and important points for QA implementation.

GCP Division, Activity Summary of the 12th Term (April 2014 – March 2016)	
Study Group	Study Group 3: Electronic
Subgroup	C-3-B
Theme	Investigations of Quality Assurance Activities for GCP Related Electromagnetic Records
<p>With the recent advances in information systematization, document digitalization compliant with legal and regulatory requirements relating to the utilization of electromagnetic records and electronic signatures, as well as with industry standards, is proceeding rapidly in the clinical trial environment in Japan. Meanwhile, there is a need for standardization of the series of activities, including reliability assurance in the digitalization process. In light of this background, we conducted the following activities to provide useful information for the practical application of QA activities for information systems used in the GCP field.</p> <p>1) “Materials for educators” relating to ER/ES and CSV</p> <p>The current state of educational methodology relating to ER/ES and CSV is far from mature compared to that for GCP. In the questionnaire survey conducted two terms ago, issues were found in the human resources development of computerized system auditing/QA managers (CSV-QA). Therefore, in the previous term, we prepared “GCP and CSV and QMS” as educational material on the concepts of GCP and CSV from the quality management perspective. This term, we prepared a follow-up of this document in the form of material for educators. The material is designed to explain the commonalities between the GCP and CSV areas to persons who are currently GCP auditors and who will be put in charge of CSV-QA.</p> <p>2) Practical understanding of “Basic concepts on the utilization of electromagnetic records in documents relating to clinical trials”</p> <p>The utilization of electromagnetic records in clinical trial documents is expected to play a role in promoting efficiency of operations relating to clinical trials. To encourage such utilization, an office memorandum was issued by the Ministry of Health, Labour and Welfare, while the Japan Pharmaceutical Manufacturers Association proposed a recommended SOP complying with this office memorandum. Momentum is building toward the implementation of clinical trial procedures which utilize electromagnetic records. In this context, we decided to organize information on issues which may be encountered by the person in charge when he or she attempts to utilize electromagnetic records in these clinical trial documents. First, we discussed each of issues which may arise from practical implementation from the standpoint of specific measures which meet the three requirements of electromagnetic records (visual readability, authenticity, and</p>	

retainability). We then examined specifically what kind of system the “cloud computing etc.” mentioned in the office memorandum is. We also summarized the points which require attention when outsourcing the destruction of relevant electromagnetic records after utilizing systems such as cloud computing.

3) Identifying and understanding trends in ER/ES regulatory requirements

In implementing quality assurance, it is important to identify the trends in regulatory requirements relating to ER/ES. We therefore continued our efforts in tracking the revisions history of MHLW Ordinance No. 44 and preparing a quick reference matrix for MHLW Ordinance No. 44 and GCP Ordinance, and notifications for their operation. In this term, owing to the revision on July 30, 2014 of MHLW Ordinance No. 44 and GCP Ordinance, we revised the “Revisions history of MHLW Ordinance No. 44,” the “Quick Reference Matrix for MHLW Ordinance No. 44 and GCP Ordinance, and Notifications for their Operation,” and “Revisions history of MHLW Ordinance No. 44 (relating to GCP).”

GCP Division, Activity Summary of the 12th Term (April 2014 – March 2016)	
Study Group	Study Group 4: Field
Subgroup	C-4-A
Theme	Communicating and Disseminating the Essence, Concepts, and Actual Initiatives for Quality Assurance of Clinical Studies and Data in Light of the Realities of Medical Institutions

While the importance of managing source documents following ALCOA principles is becoming widely recognized among parties involved in clinical trials, sponsors differ in their views on the type of source document management they require of clinical trial sites. Not infrequently, this results in confusion on the part of the medical institution. In response to this current situation, Subgroup A of Study Group 4 continued on from the activities of the previous term, attempting to prepare training materials which allow for practical learning of the ALCOA principles.

We decided to conduct a questionnaire survey of member companies etc. of the Japan Association of Site Management Organizations and the Strategic Management and Operation Network Association for Clinical Study in regard to the deliverable of the previous term, “Methods for Informing Medical Institutions of the Concept of Source Documents Based on an Understanding of the Realities of the Medical Field” (responses obtained from 30 individuals in 19 companies), and performed an overall review based on the results. To develop the training material, we reorganized the 13 cases in the previous term into 10 issues, each of which were categorized by “background,” “question,” “response,” and “commentary.” Key problems were investigated from the perspective of ALCOA principles. We also asked for feedback on day to day questions and concerns, and deliberated as much as we could on the collected information and added our comments.

Source document identification is important for assuring data quality. In some cases, the requirements and requirement levels differ according to the clinical trial sponsor (monitor), which sometimes leads to the need for more resources until database lock. To prevent this situation, we made the recommendation that it is important to shift toward identifying, at the beginning of the clinical trial, the data source documents which should be obtained, and toward sufficiently checking the preparation process, instead of organizing source documents after data is generated.

These deliberations were summarized into a poster presentation at the 15th Conference on CRC and Clinical Trials and at the 36th Annual Meeting of the Japanese Society of Clinical Pharmacology and Therapeutics, where we received a certain degree of recognition. The deliverables are scheduled to be made public on the Internet once completed.

As much as possible, we have focused on specific problematic cases in providing the commentary in this material. We hope it will be used effectively, not only as material for

training sessions, but also as real-life examples to be referred to when faced with problematic situations on site.

GCP Division, Activity Summary of the 12th Term (April 2014 – March 2016)	
Study Group	Study Group 4: Field
Subgroup	C-4-B
Theme	An Examination of the future of Quality Assurance of Investigator-initiated Clinical Trials (for NDA) and Clinical Research (for EBM)
<p>For 4-year including the previous term, Subgroup B of Study Group 4 worked on the issue of quality assurance in Investigator-initiated Clinical Trials for NDA (“CT”) and Clinical Research for EBM (“CR”). In the previous term, we deliberated on the theme, “QA/QC in CT and CR,” conducting comparison and assessment of the differences in regulations in Company-sponsored Clinical Trials for NDA, CT and CR, and investigating monitoring/auditing cases and questions relating to CT and CR.</p> <p>During this term, the Ethical Guidelines for CR (“old ethical guidelines”) and Ethical Guidelines for Epidemiological Research were integrated and issued under the title “Ethical Guidelines for Medical and Health Research Involving Human Subjects” (MEXT and MHLW Notification No. 3 issued on December 22, 2014) (“new ethical guidelines”). The characteristic of the new ethical guidelines is that quality control and quality assurance systems (monitoring and audit) for CR, which were not stipulated in the old ethical guidelines, are put into statutory form. While this development is expected to improve the reliability of CR performed in Japan, we felt that research institutions might be at a loss as to how to conduct monitoring and auditing which they had not been implementing previously.</p> <p>Therefore, we also investigated the checklist for CT and CR. In investigating this checklist, we received cooperation not only from group members but also from JSQA non-members working at research institutions. Cooperators were asked to perform a preliminary assessment of this checklist prior to it being made public on the JSQA website. This preliminary assessment of the checklist allowed us to incorporate the views of the front lines into the final deliverables. We believe this is a significant success in our approach of being “based on the realities of the front lines.”</p> <p>Similarly to the previous term, we collected information from group members on monitoring/auditing cases and questions relating to CT and CR, and deliberated on these issues. We also looked into the recruitment of public comments which took place before the issuance of the above-mentioned new ethical guidelines, and made a submission of the official views of JSQA.</p> <p>The deliverable of this term is a condensation of our activities over 2-year, and contains checklists, monitoring/auditing cases and questions relating to CT and CR, and JSQA comments submitted in relation to the recruitment of public comments which took place before the issuance of the new ethical guidelines.</p>	

GCP Division, Activity Summary of the 12th Term (April 2014 – March 2016)	
Study Group	Study Group 4: Field
Subgroup	C-4-C
Theme	An Investigation into Securing/Positioning of IRB Quality
<p>Since some time has elapsed since the deliverable of the 8th term (FY2006-2007), “What if you were appointed as an IRB member? <For non-experts and external members new to clinical trials and IRBs>,” was created, we performed an overall review of the document while incorporating the amendments made to the GCP ordinance in and after 2008.</p> <p>Amendments to the GCP ordinance were incorporated as shown below</p> <p>Before change: Pharmaceutical Affairs Law <u>After change:</u> Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics (PMD Act)</p> <p>Before change: “non-expert members,” and “external members” without interest in the hospital <u>After change:</u> “non-expert members,” and “external members” without interest in the hospital or IRB organizer</p> <p>Before change: Status of implementation on contracted enrollment <u>After change:</u> Status of implementation on clinical trial</p> <p>Before change: “Application of Standards for the Implementation of Clinical Trials on Pharmaceutical Products (Notification)” which stipulates the application of the ministerial ordinance <u>After change:</u> “Application of Standards for the Implementation of Clinical Trials on Pharmaceutical Products (Notification)” which stipulates the application of the ministerial ordinance (current “Guidance for the Ministerial Ordinance on Good Clinical Practice for Drugs (GCP Guidance)”)</p> <p>Before change: Article 1 of the Pharmaceutical Affairs Law states, “The purpose of this law is to regulate matters necessary for securing the quality, efficacy and safety of pharmaceuticals, quasi-drugs, cosmetics, and medical devices, while implementing measures relating to the regulation of designated chemicals and taking the necessary steps to promote research and development of pharmaceuticals and medical devices for which there is particularly high necessity in medical practice, and thereby improve public health and hygiene.” <u>After change:</u> Article 1 of the PMD Act states, “The purpose of this Act is to regulate matters necessary for securing the quality, efficacy and safety of pharmaceuticals,</p>	

quasi-drugs, cosmetics, medical devices, regenerative and cellular therapy products, and gene therapy products, and for preventing the occurrence or magnification of harm to public health and hygiene due to their use, while taking necessary steps while implementing measures relating to the regulation of designated chemicals and taking the necessary steps to promote research and development of pharmaceuticals, medical devices, regenerative and cellular therapy products, and gene therapy products for which there is particularly high necessity in medical practice, and thereby improve public health and hygiene.”

Before change: When an action deviating from the clinical trial protocol has been taken, the investigator must report to the sponsor, the nature of the action and the reason for the action.

After change: When an action deviating from the clinical trial protocol has been taken, the investigator must record the details in a medical chart etc.(1)

Before change: A deviation which impacts the continuation of the clinical trial or which magnifies danger to the trial subject is also reported to the hospital director and IRB.

After change: A deviation which impacts the continuation of the clinical trial or which magnifies danger to the trial subject reported to the sponsor and hospital director, and also to the IRB via the hospital director.

* The change is made to the sentence following the above passage(1), and accompanies the deletion of “sponsor” in the above passage.

New: An explanation of “conflict of interest” was added.

Points which were revised throughout the document extend over a wide range and are not mentioned herein.

GCP Division, Activity Summary of the 12th Term (April 2014 – March 2016)	
Study Group	Study Group 4: Field
Subgroup	C-4-D
Theme	Proposals based on Collection, Analysis and its Results on the Information from Stakeholders in Clinical Development
<p>Our group firstly discussed what actions to take under the theme shown above, and decided on the following two specific activities: 1. Survey on the clinical trial environment, and 2. ISO9001 vs. ICH-GCP.</p> <p>1. Survey of the clinical trial environment</p> <p>We collected information and conducted interviews on the issues troubling CRCs at the front lines of recent clinical trials (ALCOA, chart stickers, risk-based monitoring, document digitalization, hospital QMS, etc.). The interviews took place on an anonymous basis as a general rule due to our objective of discerning the true realities of the front lines. Our investigations revealed a variety of issues troubling clinical trial stakeholders including investigators, CRCs, and CRAs. Particularly prominent were problems stemming from differences in approach and interpretation of ALCOA. We hypothesized that understanding the ISO9001 process management, which underlies the concepts of quality management required in ICH-GCP, would be useful in resolving these issues.</p> <p>2. ISO9001 and ICH-GCP</p> <p>We carried out a literature review to ensure firstly that our group members understood ISO9001 itself as well as the relationship between ISO9001 and ICH-GCP. We also collected information on the ISO9001: 2015 and ICH-GCP revisions, examining their orientation and interrelations. Our investigation revealed that the revisions of ICH-GCP and ISO9001 were made with the same orientation. In relation with the ISO9001: 2015 revision, we planned and hosted a lecture by Hiroto Ishigami from BSI Group Japan on Thursday, June 4, 2015, titled “The ISO9001: 2015 Revision: Understanding ICH-GCP Quality Management.”</p> <p>3. Following up on 1 and 2</p> <p>We then decided to build on the results of 1 and 2 to create quality management training materials which would be useful for CRCs and CRAs to understand ISO9001 process management. Specifically, we aimed for material which would aid in a change of mindset, from the conventional idea of quality assurance consisting of output control of the final product, to the ISO concept of quality management through a process-based approach. We focused particularly on making our material useful for CRAs and CROs to understand the basic concepts of ISO9001 quality management, and to aid in process management at the</p>	

front lines of clinical trials.

We hope our quality management training material will be utilized effectively, leading to a resolution of the “issues troubling the clinical trial front lines” which CRCs expressed in our survey of 1 above. We feel our material can also be shared with those at the front lines of investigator-initiated clinical trials and clinical research for understanding the basic approach of quality management.

GCP Division, Activity Summary of the 12th Term (Apr 2014 – Mar 2016)	
Study Group	Study Group 5: Inspection
Subgroup	C-5-A
Theme	Information collection on GCP inspections by FDA/EMA
<p>In today’s context of clinical trials being performed on a global scale, Japanese investigator sites and sponsors may also be subjected to GCP inspections by foreign regulatory agencies. At this time, the agencies which are most likely to conduct GCP inspections in Japan and whose influence on clinical studies in Japan is relatively major are the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA). The Subgroup A, Study Group 5, GCP Division(C-5-A) separated into 3 teams to discuss the following topics.</p>	
<p>1. FDA/EMA inspection flow (Procedures Team)</p> <p>As there have been few GCP inspections conducted by the FDA/EMA to date in Japan, there is insufficient information on how these inspections are carried out in Japan. The Procedures Team therefore referred to such materials as reports from Japanese investigator sites and sponsors subjected to FDA/EMA GCP inspections in the past, the FDA’s Clinical Investigators Compliance Program Guidance Manual, and the EMA’s Inspection Procedures. On the basis of these materials, the team summarized the flow of the inspection procedures in Japan in three parts: pre-inspection preparations, actions and responses during the inspection, and post-inspection communications.</p>	
<p>2. New notifications from authorities relating to GCP and/or inspections (New Notifications Team)</p> <p>This team collected information on new regulations and guidelines on clinical trials from websites such as “In The News” (FDA) and “News and updates” (EMA). The list of collected information is published and updated on the JSQA website. The team also created the summary sheet for the regulation/guideline which meets the pre-defined criteria based on the importance and impact to us.</p> <p>In particular, the team created English-Japanese bilingual document and explanatory materials for EU Clinical Trial Regulation (REGULATION (EU) No 536/2014, EU-CTR) which is significant deregulation and streamlining as this regulation has major impact to the clinical trials in Japan.</p>	
<p>3. Case studies of FDA warning letters (Case Study Team)</p> <p>Out of Warning Letters made public by the FDA between May 9, 2013 and April 1, 2015, 32 letters (containing a total of 85 warnings) issued to investigators, sponsors, or IRBs in</p>	

relation to GCP (pharmaceuticals and medical devices) were analyzed by the Case Study Team. An Excel database was created and uploaded to the JSQA member website. The majority of warnings were concerning the investigator's responsibilities and record retention, and unlike Japan, FDA clearly requires the investigator's responsibility for execution of the clinical trial. The team also made a case study presentation titled "Learning from FDA Warning Letters: Key Points of Inspections" at the 35th What's a Quality & Compliance? - Review Meeting on Case Examples of Compliance Reviews/Inspections (held in March 2015).

In addition, C5A organized ten lecture meetings by external professionals regarding overseas clinical studies and inspections mainly for the members of Study Group 5.

GCP Division, Activity Summary of the 12th Term (April 2014 – March 2016)	
Study Group	Study Group 5: Inspection
Subgroup	C-5-B
Theme	An Investigation of the Clinical Trial Environment and Regulatory Requirements in China and Korea
<p>Background</p> <p>In recent years, implementing clinical trials in Asian countries is becoming commonplace for companies based in Japan, and occupies an important strategic position in terms of pharmaceutical development for them. Changes in the Asian clinical trial environment occur quickly, and constant vigilance is called for. However, there is limited public information on clinical trials in Asian countries including China and Korea, and not a few companies and managers appear to be struggling to obtain the desired information. In this context, the JSQA set up a study group for Asia in the 9th term (2008-2009), and has since carried out activities for 4 terms including the present term.</p> <p>Purpose</p> <p>This term, we focused on China and Korea due to the preference of many of our members. We aimed to obtain the latest updates on regulatory matters and investigate more specific inspection findings.</p> <p>Method</p> <p>The governments in the two countries of our focus are reinforcing their promotion of clinical trials, and we felt that trend watching of the swiftly changing environment was crucial. Therefore, both the China and Korea Teams identified local materials with high value reflecting the latest situation, translated them into Japanese, and examined their contents carefully.</p> <p>Results</p> <p>We released the latest laws, guidelines, supervisory frameworks, and inspecting information relating to clinical trials. We also released information on the techniques we used for searching local websites during our activities this term, in the hopes that it would help JSQA members in their search for information.</p> <p>Main content of deliverables</p> <ol style="list-style-type: none"> 1. China <ul style="list-style-type: none"> - Laws and regulations on clinical trials - Supervisory and management systems for clinical trials 	

- Types of inspections and overview of implementation
 - List of inspection findings
 - Comparison of CFDA, FDA, and PMDA inspection findings
 - In addition to the above, we held an internal lecture to which we invited local CRO managers, and released the content of the Q&A session.
2. Korea
- Supervisory and management systems for clinical trials
 - (K-GCP, essential documents, human research protection program, guidelines for clinical trial electronic data processing and management)
 - Basic plan for clinical trial site inspection 2015
 - Analysis of approval status for clinical trials in 2014

GCP Division, Activity Summary of the 12th Term (April 2014 – March 2016)	
Study Group	Study Group 5: Inspection
Subgroup	C-5-C
Theme	Inspection Management in the Compliance Review
<p>During this term, Subgroup C of Study Group 5 (“our group”) worked on the theme of “Inspection Management in Compliance Review,” investigating GCP on-site inspections and document-based conformity inspections (“compliance reviews”) conducted by the Pharmaceutical and Medical Devices Agency (“PMDA”) to achieve the following two objectives:</p> <ul style="list-style-type: none"> - To create a list of conceivable questions for mock inspections. - To create a procedure for the preparation of compliance review, covering the period from the stage of conduct of clinical trials to the day of inspection, and the handling procedure at the compliance review. <p>We conducted a questionnaire survey of the members of our group (“members”) on issues in inspection management and what kinds of know-how they wished to obtain. The results of this questionnaire, we conducted the study and the creation of our report.</p> <p>Questionnaire responses on mock inspections indicated the demand of sponsors for knowledge of how to implement them efficiently. Especially, unexperienced applicants wanted know-how on mock inspections because they had little accumulation of information for this topic. Others told of their experiences of mock inspections which were of little use, as the questions asked were far removed from ones of the actual compliance review. Therefore, we reasoned that preparation of a list of questions in line with the actual contents of compliance review would enable us to conduct the mock inspection more practically and efficiently. We collected questions on the basis of records of compliance reviews over the last 5 years at the eachcompanies our members belong. We categorized these questions according to the items in the “New Drug GCP On-site Inspection and Document-based Conformity Inspection Checklist (For Clinical Trial Sponsor)” and further compiled a “the conceivable questions for mock inspection” which contains examples of materials to have ready in preparation for responses.</p> <p>Regarding the creation of a procedure for the preparation of compliance review, covering the period from the stage of conduct of clinical trials to the day of inspection, and the handling procedure at the compliance review, the factors to be included in our reports proposed in the opinions put forward by many of our members are following.</p> <ul style="list-style-type: none"> - Knowledge of the key points for scheduling of operations, - Consideration for efficiency, including timelines for various required tasks. 	

- Making of a standard procedure for preparing for and dealing with the compliance review.

Besides, other responses also suggested that keeping the compliance review in mind during the conductance of clinical trial should lead to better efficiency in preparing for and dealing with the compliance review.

On the basis of these opinions, we created a flow chart of operations, responses, and preparations from the clinical trial to completion of the compliance review. Questionnaire responses on successfully completed compliance reviews and efficiency measures were also incorporated into the flow as key operational points etc. we also added filled-out samples of forms to be submitted prior to the compliance review, and useful examples of site layout drawings etc. for the day of the compliance review.

We expect our report to assist both inexperienced and experienced applicants in preparation for and handling of compliance reviews, making smooth for the formers and more efficient for the latters. We also hope our “conceivable questions for mock inspection” will make the applicants possible to conduct practical and efficient mock inspections, and be of some help to them for organizing the viewpoints of recent compliance reviews and identifying problems in daily operations, regardless of whether the user implements a mock inspection or not.

GCP Division, Activity Summary of the 12th Term (April 2014 – March 2016)	
Study Group	Study Group 5: Inspection
Subgroup	C-5-D
Theme	Quality Control and Quality Assurance of Contracted Operations
<p>Due to the revision of 1997 MHLW Ordinance No. 28 "The Ordinance on Good Clinical Practice," it is now possible to contract all of the operations relating to carrying out and managing the clinical trial. Needless to say, the sponsor and contract research organization (CRO) must go beyond their conventional relationship of contract giver and contractee, with the two parties deepening their mutual understanding and trust to form a partnership in pharmaceutical development. In recent years, there are more cases of some of the development operations being re-contracted from one CRO to another, and the execution of quality control and quality assurance compliant with GCP requirements is becoming more diverse depending on the form of the contracted operation. Therefore, in Subgroup D of Study Group 5, we repeatedly brainstormed and deliberated on which themes to focus on relating to "quality control and quality assurance of outsourced operations." We decided on the following 4 themes and performed activities accordingly.</p> <p>I Exploring the causes of the different mindset between sponsor and CRO</p> <p>There are cases in which contracted operations can give rise to contractual or operational problems between the sponsor and CRO or, even when not manifesting as a problem, be performed with neither party feeling dealt with fairly, due to bilateral lack of communication or discrepancies in understanding. We hypothesized that the cause of such situations is the different mindsets of the two parties in regard to quality of operations. On the basis of problematic cases collected through a questionnaire survey of group members, we discussed the causes of this discrepancy.</p> <p>II Investigation of the current situation of contracting to CROs outside Japan</p> <p>With the increase in offshore and/or international joint development, the importance of contracting foreign clinical trial operations and regulatory applications to foreign CROs is rising. We therefore presented the results of a questionnaire survey of group members on "quality management," "source documents," and "audit" in relation to contracting operations to foreign CROs, highlighting the points which require attention at the time of contracting and adding our comments on risks which require caution in specific forms of contracting (total contracting, partial contracting, total re-contracting, partial re-contracting).</p> <p>III Relationship between sponsor and contractee: Organizing past problems and considering new issues</p>	

Effective measures to address problems in contractee selection and management have yet to be established, despite a range of proposals made by various business associations to date, and the JSQA's repeated investigations into cases of sponsor-CRO problems and explorations of what is appropriate in terms of the sponsor-CRO relationship. In addition, legal amendments and new notifications have changed the clinical trial landscape since our investigations took place. In this context, we reevaluated our results to date, and used the results of our questionnaire survey of group members to deliberate on the new issues of "re-contractee management" and "contracting of storage/delivery of pharmaceuticals." Thus we discussed appropriate contracting relationships and methods for the selection and management of contractees.

IV Status surveys of "on-site inspections of CROs" and "contracting of audit operations"

The quality of operations carried out by a contracting CRO must be assured by the sponsor in some way. One such means is the on-site audit of the CRO. This term, we conducted a questionnaire survey to understand the current realities of on-site audits of CROs, and will report the results. We will also present the results of our questionnaire survey on the situation of contracted audits, as despite recent cases of the audit itself being contracted to an external entity, information on such contracted audits is extremely limited.

GCP Division, Activity Summary of the 12th Term (April 2014 – March 2016)	
Study Group	Special Project Group 1
Subgroup	C-T-1
Theme	Examination of Case Examples of Compliance Reviews/Inspections
<p>Special Project Group 1 collected, examined, and analyzed 143 PMDA compliance reviews from Japan and overseas contributed by members of the JSQA GCP Division, and 100 case examples of compliance reviews obtained from PMDA by using the Law Concerning Access to Information Held by Administrative Organs. We also collected and examined the case example of an inspection by an overseas regulatory authority reported from member, as well as relevant regulatory information mainly from public sources. We presented our results as feedback to JSQA members at the annual “What’s a Quality & Compliance? – Review Meeting on Case Examples of Compliance Reviews/Inspections –.”</p> <p>1) Conferences</p> <p>(1) What’s a Quality & Compliance? – Review Meeting on Case Examples of Compliance Reviews/Inspections–</p> <p>35th Meeting: March 20, 2015, Nissho Hall, Tokyo (attendance: approx. 700)</p> <ul style="list-style-type: none"> – Case examples of compliance reviews by PMDA (including the results of deliberations by Special Project Group 1) – PMDA special lecture: Current situation and future prospects of compliance reviews – Invited lecture: Experience with EMA Inspections – Trends in inspections by overseas regulatory authorities (including presentation by C-5-A on Warning Letters) <p>36th Meeting: March 4, 2016, Nissho Hall, Tokyo (expected attendance: approx. 700)</p> <ul style="list-style-type: none"> – Case examples of compliance reviews by PMDA (including the results of deliberations by Special Project Group 1) – Trends in inspections by overseas regulatory authorities – Invited lecture: Experience with FDA/EMA Inspections – Panel discussion on misconductsin clinical trials <p>(2) Website-based basic course</p> <p>To give persons inexperienced with compliance reviews a better understanding at the Review Meeting on Case Examples of Compliance Reviews/Inspections, we developed a basic course offering information on compliance reviews, and made it accessible year round on the JSQA website.</p>	

2) Deliverables

- Database of case examples of compliance reviews collected using the Law Concerning Access to Information Held by Administrative Organs [released on the JSQA website]
- Summary of deliberation results (35th and 36th Meetings) [distributed to Meeting participants and to companies which contributed case examples]
- GCP compliance review reports (35th and 36th Meetings) [distributed to Meeting participants (GCP Division members only) and to companies which contributed case examples]

GCP Division, Activity Summary of the 12th Term (April 2014 – March 2016)	
Study Group	Special Project Group 2
Subgroup	C-T-2
Theme	The Planning, Development, and Implementation of GCP Training Courses for Personnel in Charge of Clinical Trials
<p>We held 7 types of GCP training courses for personnel in charge of clinical trials. The courses ran for a total of 11 sessions over a term of 2 years.</p> <p>The GCP training courses were designed to provide knowledge necessary for the process of clinical trial quality control and quality assurance, and to improve the skills of participants. The courses successfully achieved their purpose.</p> <p>Through their participation in course development, the members of Special Project Group 2 deepened their knowledge and understanding of GCP quality control, audits, and quality assurance, and were able to upgrade their own skills.</p> <p>For the purpose of course development, Special Project Group 2 members met once monthly for a total of 24 meetings over 2 years.</p> <p>Overviews of courses</p> <p><u>QC/QA Beginners' Course (Offered twice: July 2014 and July 2015)</u></p> <p>1-day course, maximum enrollment 80 people</p> <p>This course was offered to persons new to clinical trial operations and to those who wished to check on the basics. Designed to give participants a basic knowledge of QC/QA in the GCP area, the course consisted of lectures in “Overview of QC/QA” and “Overview of the Pharmaceutical Affairs Law and GCP,” plus a “Q&A Session.”</p> <p><u>QC Basic Course (Offered twice: December 2014 and December 2015)</u></p> <p>1-day course, maximum enrollment 42 people</p> <p>This course was offered to persons with 1 to 3 years of experience in GCP QC or monitoring operations. The sessions featured a lecture titled “Practice and Overview of Quality Control” with a focus on quality control operations for “clinical trial documents etc.,” plus group discussions of case study exercises.</p> <p><u>QC Advanced Course (Offered twice: July 2014 and July 2015)</u></p> <p>1-day course, maximum enrollment 42 people</p> <p>This course was offered to persons in charge of the practicalities of GCP quality control or monitoring (participants had to be able to take part in discussions on the basis of their company’s QC operation criteria (essential documents)). The course mainly featured group</p>	

discussions based on the quality control experiences of each participant.

QA Basic Course (Offered twice: December 2014 and December 2015)

1-day course, maximum enrollment 60 people

This course was offered to persons with less than 3 years' experience in GCP audit operations, and consisted mostly of classroom-style learning of "Introduction to GCP audit," "Case study exercises," "Introduction to GCP audit operations in actual companies (personnel from 2 companies introduced their respective firms' positioning of the audit division and the practical work of auditing)," and "Panel discussion."

Upgrading of Interview Skills Course (Offered once: March 2015)

1-day course, participation approx. 30 people

The course was offered for the purpose of upgrading the interview skills of persons in charge of clinical trials and consisted of a lecture titled "Improvement of Practical Interview Techniques and Use in Audit Operations" and hands-on interview exercises with case studies.

QA Advanced Course (Offered once: February 2015)

2-day course, participation approx. 25 people

This course consisted mainly of group work (role-playing) about a mock audit of a clinical trial sites, and was offered for the purpose of upgrading the skills necessary for auditing clinical trial sites, including the thinking process, information collection through review of clinical trial documents or records and through interviews, and organization of the information gained. Through the cooperation of Hamamatsu University School of Medicine, participants were given the unique opportunity of interviewing hospital personnel with clinical trial experience.

Communication Skills Training (Offered once: February 2016)

2-day course, maximum enrollment 36 people

This course consisted mainly of hands-on exercises and was designed to upgrade the communication skills of personnel involved in clinical trials.

Offered for the first time this term, the course had a lecture component on communication and interviewing, and a hands-on component with a repetitive cycle of role-playing on possible clinical trial scenarios and feedback on the role-playing.

Through the cooperation of Hamamatsu University School of Medicine, participants were given the unique opportunity of communicating with hospital personnel with clinical trial experience.

GCP Division, Activity Summary of the 12th Term (April 2014 – March 2016)	
Study Group	Special Project Group 3
Subgroup	C-T-3
Theme	Submission of Public Comments and Notification of the Contents of Amendments to GCP etc.
<p>1) Submission of public comments</p> <p>We deliberated on the following matters for which public comments had been recruited, and submitted our results to the Ministry of Health, Labour and Welfare (MHLW) as official comments of JSQA.</p> <ul style="list-style-type: none"> - Comments on the “Cabinet Order for the Partial Revision of the Regulations for Enforcement of the Pharmaceutical Affairs Act (draft)” etc. - Comments on the “Ordinance for the Partial Revision of the Ordinance on the Standards for the Implementation of Clinical Trials (GCP Ordinance) (tentative name, draft)” (draft framework) <p>We deliberated on the following matter for which public comments had been recruited, but determined that submission of comments was unnecessary.</p> <ul style="list-style-type: none"> - Comments on the draft addendum to the ICH E6(R2) GCP guidelines <p>For the following matter, we submitted to the MHLW, comments which were compiled by another group.</p> <p>Recruitment of public comments regarding “Ethical Guidelines for Medical and Health Research Involving Human Subjects (draft)”</p> <p>We also compiled the procedures for summarizing public comments within JSQA and released it on the JSQA website.</p> <p>2) Notification of details of amendments to GCP</p> <p>The “Japanese Association of Clinical Study Textbook (JACST)” and our group jointly prepared the following educational materials for the purpose of clearly understanding the amendments, and uploaded them to the JSQA website for the general public.</p> <ul style="list-style-type: none"> - A table comparing each provision of the GCPs for pharmaceuticals, medical devices, and regenerative medicine products - Material indicating the “background of differences among the three GCP ordinances” <p>3) We prepared explanatory documents for the Notice from the Evaluation and Licensing Division “Basic Concept of Using Electromagnetic Records in Clinical Study-related</p>	

Documents” issued as of July 1, 2013, and uploaded them to the JSQA website for the general public.

GCP Division, Activity Summary of the 12th Term (April 2014 – March 2016)	
Study Group	Special Project Group 4
Subgroup	C-T-4
Theme	Responding to Lecture Requests to the GCP Division, and Managing and Maintaining Lecture Materials
<p>Special Project Group 4 of the GCP division (C-T-4) began its activities in 2013 based on the theme in the title, and in this 2nd term, we acted with the aim of achieving the following objectives.</p> <p>1. Purpose of activities</p> <ul style="list-style-type: none"> - To respond to “requests for lectures” received by the GCP Division on the basis of the manual prepared in the previous term, implementing appropriate administrative procedures, processing and managing presentation materials and reviews, revising internal rules to better reflect the current realities, and exercising continuous management. - To create mechanisms for the appropriate storage and management of “lecture materials” (“resources”) held by the GCP Division, as well as internal rules for constructing such a system. - Inspect past resources and, as with new resources, exercise appropriate storage and management on the basis of the internal rules above. <p>2. Details of activities</p> <ul style="list-style-type: none"> - Revision of “Internal Rule 01: Approval of Lecture Implemented by GCP Division” (Ver. 2: 2015/7/24) Main revision: Change of stipulated range, and revision of forms etc. to better reflect the current realities. - Responding to requests for lectures on the basis of the revised Internal Rule 01. - Formulation of “Internal Rule 02: Storage of Lecture Materials” (Ver. 1: 2015/7/24) We formulated procedures relating to the storage of resources prepared by the GCP Division. - On the basis of this Internal Rule, we stored the materials prepared over the past 2 years and new materials. 	

GCP Division, Activity Summary of the 12th Term (April 2014 – March 2016)	
Study Group	Special Project Group 5
Subgroup	C-T-5
Theme	Creation of the Guideline for Global Auditing Appendix (Trilateral Agreement)
<p>JSQA GCP Division Special Project Group 5 held repeated discussions on the 9 Appendices which follow the Global Guideline for GCP Audit trilaterally agreed upon by SQA, RQA, and JSQA. The outcomes were presented through a panel discussion at the 4th Global QA Conference held in Las Vegas in April 2014.</p> <p>The Japanese explanatory version of The Global Guideline for GCP Audit, published in 2010, was revised to reflect the changes made in April 2012 and April 2014, and uploaded to the JSQA member website together with the Japanese version of the Appendices.</p> <p>SQA, RQA, and JSQA have each released on their websites, these Guidelines and Appendix created as the shared understanding of the persons in charge of audits. We hope they will be utilized actively.</p> <ul style="list-style-type: none"> ● Past project activities (2005 – 2014) <p>2006: Deliverable of GCP Division Special Project Group 1: “Guideline for GCP Auditing” (Document No. 05C10)</p> <p>2007: Submitted a manuscript titled “The Guideline for GCP Auditing” to Clinical Evaluation, and a manuscript titled “The JSQA Guideline for GCP Auditing” to QA Journal</p> <p>2009: Reached a trilateral agreement with SQA, RQA, and JSQA on The Global Guideline for GCP Audit and released it on the JSQA member website</p> <p>2010: Released the explanatory version of The Global Guideline for GCP Audit on the JSQA member website</p> <p>2012: Revised The Global Guideline for GCP Audit</p> <p>2014: Reached a trilateral agreement with SQA, RQA, and JSQA on the 9 Appendices, and presented them through a panel discussion at the 4th Global QA Conference. Released the Japanese version of the Appendices together with the explanatory version of The Global Guideline for GCP Audit on the JSQA member website.</p> <ul style="list-style-type: none"> ● Contents uploaded to the JSQA member website <p>The Global Guideline for GCP Audit and Appendices</p> <p>The Global Guideline for GCP Audit: Explanatory version revised September 2014</p> <p>Appendix 01 Risk-Based Approach for Audit Planning</p> <p>Appendix 02 Corrective and Preventive Action</p>	

Appendix 03 Grading of Audit Findings

Appendix 04 Clinical Investigator Site Audit

Appendix 05 Electronic Medical Records (EMR)

Appendix 06 Conducting an IRT (IVRS/IWRS) Vendor Audit

Appendix 07 Conducting Audits of Data Management or Electronic Data Capture Systems

Appendix 08 CRO Audit

Appendix 09 Audit for IRB/IEC

GCP Division, Activity Summary of the 12th Term (April 2014 – March 2016)	
Study Group	Special Project Group 6
Subgroup	C-T-6
Theme	Publication of the Revised “<i>Shokai GCP Shorei (Full Commentary on GCP Ordinance)</i>” (JSQA ed.)
<p>The first edition of “<i>Shokai GCP Shorei (Full Commentary on GCP Ordinance)</i>” (JSQA ed.) was published in November 2009.</p> <p>After the publication, the GCP Ordinance was partially revised in December 28, 2012 and August 6, 2014.</p> <p>We therefore decided to publish a revised edition, for the purpose of carefully examining the details of each provision of the GCP Ordinance including the course of the partial amendments made after the publication of the first edition, and while comparing with the contents of ICH-GCP as much as possible, providing commentary on where the true meaning shown in each provision lies, and clarifying the matters in each GCP provision which persons involved in clinical trials should keep in mind.</p> <p>We deliberated on the content of the revised edition, and published the 2nd Edition in June 2015.</p>	