GCP Division, Activity Summary of the 14th Term (April 2018– March 2020)	
Study Group	**Study Group 1: Self-enlightenment**
Subgroup	**C-1-A-1**
Theme	**Outline of QMS for self-development —Clinical trials of pharmaceuticals (including investigator-initiated clinical trials)—**

This subgroup started its activities, aiming to self-develop and work product creation to understand overall elements, including new requirements associated with the issuance of ICH-E6 (R2), which are necessary for the establishment of the outline of the quality management system (QMS) for clinical trials from a broader viewpoint. Before the realization of the subgroup's discussion, needs from the members in the subgroup were summarized. The summarization revealed that the members wished to understand, not specific methods, but overall elements necessary for implementation of the QMS in their companies and the significance of those elements, from a broader viewpoint. On the basis of such opinion, the discussion was started. The subgroup began with a discussion about the reason for requirements for each element required by the Enhancing Quality and Efficiency in Clinical Development Through a Clinical QMS Conceptual Framework: Concept Paper and understanding the rationale of the requirements. The subgroup then discussed tools for realization for each element, for reference in implementing the QMS. The tools can be chosen or changed, for reference in implementing the QMS in each company, considering that the company's scale and guidelines vary in terms of the realization of requirements for the QMS.

The subgroup also discussed methods for implementing systems for risk and issue management.

GCP Division, Activity Summary of the 14th Term (April 2018– March 2020)	
Study Group	**Study Group 1: Self-enlightenment**
Subgroup	**C-1-A-2**
Theme	**QMS practice for self-development —Practice and investigation using a risk management tool—**

Under the theme "QMS practice for self-development—Practice and investigation using a risk management tool—," Team 2, Subgroup A, Study Group 1 (hereinafter referred to as the subgroup) started its activities. As new requirements, the ICH-E6 (R2) guidelines specify that the sponsor should implement a quality management system (QMS) and that the QMS should use a risk-based approach (RBA). Each member company in the subgroup is establishing a QMS but does not have any experience with "Critical Process and Data Identification, Risk Identification, Risk Evaluation, Risk Control, Risk Communication, Risk Review, and Risk Reporting" required for the RBA in actual clinical studies. Therefore, they expressed an opinion that they wanted to use existing protocols to investigate the QMS-RBA.

The subgroup prepared several existing protocols through "ClinicalTrials.gov," a clinical study database provided by the U.S. National Institutes of Health and the U.S. Food and Drug Administration, to investigate the QMS-RBA for each clinical study, which would lead to our self-development for the QMS. The Risk Assessment and Categorization Tool (RACT) provided by TransCelerate was used as a risk assessment tool. For obtaining a common understanding among the subgroup members, it would be necessary to unify the concept of issues and risks among the members before investigation. After issue cases were solicited from the members to share the information about how risks can be managed, protocol investigation was initiated using the RACT. Although the description of the RACT is generalized to ensure that the tool can be used in any studies, users should be familiarized to the assessment method of the RACT. Thus, we further investigated the protocols while adding notes and cases as necessary, thereby formulating a deeper common understanding among all members. The results of our investigation and the additional version of the RACT were unpublished deliverables because they contain substantial amount of confidential information of other companies and was only shared within each subgroup member company.

GCP Division, Activity Summary of the 14th Term (April 2018– March 2020)	
Study Group	**Study Group 1: Self-enlightenment**
Subgroup	**C-1-A-3**
Theme	**Investigation of group auditing**

In FY2016 to 2017 of the 13th term, Subgroup D of Study Group 2 (C2D) proposed group auditing as an efficient method for system auditing in contract research organizations, and group audits were conducted for system vendors and laboratory test companies. The results suggest that group auditing is a more useful method with a higher satisfaction level of auditors (sponsors) in terms of "the quality of audits," "efforts on audits," and "expenses for audits" than usual auditing by each sponsor. Taking over the activities of the C2D group in the 13th term, Subgroup A-3 of Study Group 1 carried out the following four activities during the 14th term and summarized the results in a deliverable:

(1) To examine the system of highly practical and effective group audits, we exchanged opinions with auditees to collect the information on current problems on sponsor's audits and expectations for group auditing.
(2) We investigated points to be improved and considered for audit methods that had been identified in the group audits conducted in the 13th term and investigated standard operating procedures (SOPs).
(3) We proposed future issues on group auditing and plans for the widespread use of group auditing.
(4) To disseminate the information on group auditing, we submitted a paper on the group audits conducted in the 13th term for publication to the "Japanese Journal of Clinical Pharmacology and Therapeutics."

GCP Division, Activity Summary of the 14th Term (April 2018– March 2020)	
Study Group	**Study Group 1: Self-enlightenment**
Subgroup	**C-1-B**
Theme	**Q&A on first medical device clinical trials and regenerative medicine products**

The "Ministerial Ordinance on Good Clinical Practice for Medical Devices" (hereinafter referred to as the "Medical Device GCP") came into effect in March 2005. In the 8th term (2006 to 2007), GCP Division of the Japan Society of Quality Assurance (JSQA) established a study group to investigate clinical studies of medical devices. In the activities during six terms over the past 12 years, we aimed at improving the "quality" of clinical trials of medical devices. Although the "Ministerial Ordinance on Good Clinical Practice for Regenerative Medicine Products" (hereinafter referred to as the "Regenerative Medicine GCP") came into effect in July 2014, the JSQA did not have any study group to investigate clinical studies of regenerative medicine products. In the present term, we combined regenerative medicine products with medical devices to establish a group to investigate "clinical trials for medical devices and regenerative medicine products (including investigator-initiated trials)" and started to determine a study theme on reliability assurance in clinical studies of medical devices and regenerative medicine products.

The latest revision of the Medical Device GCP as of December 2019 was a partial change in the definition of post-marketing clinical studies in July 2017, with no revision of the Medical Device GCP during the present term. No new topics were available on the Medical Device GCP, making it difficult for us to determine the study theme of the present term. In a group meeting, an opinion was voiced that the existing themes should be improved in quality. With regard to the Regenerative Medicine GCP, although we wanted to investigate reliability assurance based on actual cases, it was also difficult to determine a study theme on the Regenerative Medicine GCP because few participating members had experience with the Regenerative Medicine GCP and thus had difficulty in exchanging opinions and little information on cases related to the Regenerative Medicine GCP were available.

As the theme (activities) of the present term, we eventually determined to provide problems and problematic cases experienced by each group member in clinical trials of medical devices, extract inquiries (questions) raised in clinical trials of medical devices, discuss solutions and advices (answers), and summarize the results in a Q&A format in a deliverable, as with the previous (13th) term. Note that medical device manufacturers are less likely to conduct clinical trials than drug manufacturers because the market of medical devices is smaller and medical devices are continuously improved after marketing approval and these changes do not require the conduct of clinical trials. We thus focused on inquiries raised during first clinical trials to extract questions. In addition to questions on the Medical Device GCP, we also investigated questions that were also covered by the Regenerative Medicine GCP to formulate their answers.

Through these activities, we successfully extracted questions on the following (1) to (3) matters and formulated their answers. These results were summarized in a Q&A format in the deliverable:

(1) Education and training
(2) Sponsor's system
(3) Management of accessories of investigated medical devices

GCP Division, Activity Summary of the 14th Term (April 2018– March 2020)	
Study Group	**Study Group 1: Self-enlightenment**
Subgroup	**C-1-C**
Theme	**Clinical Trials Act—Its overview and gap analysis between the act and ICH-GCP/Ethical Guidelines—**

The common code for medical research in humans is the Declaration of Helsinki. In Western countries, general clinical researches involving intervention are conducted under the control of the Good Clinical Practice (GCP) agreed by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) (hereinafter referred to as the "ICH-GCP"). In Japan, clinical trials for Investigational New Drug (IND) and post-marketing clinical studies have been conducted in accordance with the "Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics" and the "Ministerial Ordinance on Good Clinical Practice for Drugs" (hereinafter referred to as the "J-GCP"). Other clinical researches have been conducted according to the "Ethical Guidelines for Medical and Health Research Involving Human Subjects" (hereinafter referred to as the "Ethical Guidelines"); however, there have been concerns about conducting clinical researches based on non-legal guidelines.

Between 2012 and 2014, scandals on clinical research were discovered in succession, which destroyed the public reliability of clinical research. To restore the reliability that was lost, clinical researches had to be conducted in compliance with any acts, and therefore, the Clinical Trials Act (hereinafter referred to as the "Act") was established (promulgated on April 14, 2017, and enforced on April 1, 2018).

Several government and ministerial ordinances, notifications, and Q&A lists have been issued to stipulate the detailed operation of the Act. However, previous clinical researches, including clinical trials for IND, have been mainly based on the J-GCP or the Ethical Guidelines, as described above, and thus, some physicians who have been involved in clinical researches based on these rules may be confused with their differences or may not be able to fully understand the Act.

Based on the background, Subgroup C of Study Group 1 in the 14th Term determined to develop explanatory materials to help understand the Act mainly for physicians involved in "specified clinical trials." In our activities, the group members were divided into the following three teams according to the objective:

[Team A]

Summarization of the Clinical Trials Act (overview)

Focusing on "specified clinical trials", which must be conducted in compliance with the Act, Team A extracted the information that should be known by physicians responsible for "specified clinical trials" to prepare slides using Microsoft PowerPoint (Attachment No. 19C05-1). In particular, the management of conflict of interest was explained in detail because it triggered the establishment of the Act. We also created a separate list using Microsoft Excel to clarify the flow of a clinical research (Attachment No. 19C05-2).

[Team B]

Gap analysis between the Clinical Trials Act and the ICH-GCP

Team B analyzed gaps between the ICH-GCP, which regulates general clinical researches

involving intervention in Western countries, and the Act; compared them with regard to terms, items (Articles), and documents (Protocol and ICF) using Microsoft Excel; and summarized the results in a list (Attachment No. 19C05-3).

[Team C]

Gap analysis between the Clinical Trials Act and the Ethical Guidelines

Team C analyzed gaps between the Ethical Guidelines, which had been the basis of clinical researches involving intervention until the Act was established in Japan, and the Act; compared them with regard to terms, items (Articles), and documents (Protocol and ICF) using Microsoft Excel; and summarized the results in a list, as with Team B (Attachment No. 19C05-4).

GCP Division, Activity Summary of the 14th Term (April 2018– March 2020)	
Study Group	**Study Group 2: Electronic**
Subgroup	**C-2-A**
Theme	**Investigation of quality assurance for using clinical trial management systems (EDC, IWRS, CTMS, eTMF, etc.)**

Subgroup A of Study Group 2 in GCP Division in the 14th term focused on the "Investigation of quality assurance for using clinical trial management systems (EDC, IWRS, CTMS, eTMF, etc.)." The group members were divided into two working groups according to individual objectives of participation. The [Working Group 1] focused on increased efficiency and effective use of EDC, IWRS, and CTMS and investigated the "roles of quality control and auditing for assuring the quality of IT systems involved in clinical trials." The [Working Group 2] examined the "current status of eTMF operation and discussion about that" to identify issues raised after the introduction of eTMF and measures to solve the issues and provide proposals for improving eTMF.

[Working Group 1]

Working Group 1 of Subgroup A worked under the theme of the roles of quality control and auditing for assuring the quality of IT systems involved in clinical trials (hereinafter referred to as the "IT systems").

We first investigated the current status of IT system utilization (definition and type of the IT system, related duties, issues about the use of the IT system, and related regulatory trends).

Based on the results, we investigated measures to solve the issues about the use of IT systems and eventually summarized the results according to two themes: 1) "investigation of issues about IT systems and measures to solve the issues" for departments that conduct clinical trials and 2) "discussion of the roles of auditing in terms of computerized system validation (CSV)" for departments that audit clinical trials.

As regards the first theme, we presented individual and common issues about IT systems and the measures to solve the issues, as well as expectations on the coordination of IT systems and the "system integrated model," issues, and measures. As regards the second theme, we presented CSV audits, audits that cover more than one IT system, points to be considered for CSV, and common cases, in terms of the form, operation, and design of IT systems and differences between IT vendors and users.

The efficient use of IT systems, which was investigated in the present term, is very important because ensuring data integrity and consistency is required for drug development.

[Working Group 2]

Given that the eTMF system is newer than EDC and other systems and has not been spread to the entire industry, each company may have little experience and shared information and may be using the system by trial and error.

Taking the situation into consideration, Working Group 2 of Subgroup A worked under the theme of quality assurance of eTMF and the current status of eTMF use. We first assigned a member with knowledge of eTMF to a lecturer and held a study meeting to examine and discuss regulatory requirements for eTMF. To clarify the actual situation of operational methods after the introduction of eTMF systems and methods for controlling the quality of TMF, a questionnaire survey was also conducted among representative members of GCP Division of the Japan Society of Quality Assurance.

To prepare a deliverable, we summarized regulatory requirements for TMF and related discussion, results of the questionnaire survey, and results of investigation on methods for operating eTMF systems effectively and efficiently. We hope that the deliverable will be used to consider operation methods after the introduction of eTMF, regardless of whether eTMF has already been used.

We believe that the measures and proposals presented here will contribute to quality assurance for using the clinical trial management systems (EDC, IWRS, CTMS, eTMF, etc.).

GCP Division, Activity Summary of the 14th Term (April 2018– March 2020)	
Study Group	**Study Group 2**
Subgroup	**C-2-B**
Theme	**Collection of clinical study data using IT**

We first conducted a case study in medical institutions to examine clinical studies using data collected by IT and shared the information and then determined to extract issues on data collection and issues in laws and regulations for ensuring data reliability and investigate them.
Focusing on mobile device systems expected to be used in clinical studies, such as big data, artificial intelligence (AI), and Internet of Things (IoT), we investigated how they can be used in clinical studies and what should be considered for using them. To understand the current status in Japan, we conducted a questionnaire survey on data collection using mobile devices in clinical studies. We also extracted and discussed issues raised when mobile devices were installed and issues in laws and regulations and summarized the results of the following three activities in a deliverable:

(1) We investigated the reliability assurance of data handled by “Devices&Apps,” which is expected to be widely used for designing and conducting clinical studies, among the four eSource categories defined by TransCelerate.
(2) We conducted a questionnaire survey among member companies of GCP Division of the Japan Society of Quality Assurance, compared the situation in Japan with that in foreign countries, and organized issues to discuss prospects.
(3) Regarding the conduct of clinical studies using mobile devices, we investigated regulatory requirements that are in effect in Japan and overseas.

GCP Division, Activity Summary of the 14th Term (April 2018– March 2020)	
Study Group	**Study Group 3: Reliability Assurance**
Subgroup	**C-3-A**
Theme	**CAPA in the GCP area -Investigation of RCA/cases and preparation of educational materials -**

C3A, our group started to work with two keywords, “examination cases” and “corrective action and preventive action (CAPA),” and the group members were divided into four independent working groups to explore their respective themes.

The CAPA Root Cause Analysis (RCA) Working Group discussed and proposed effective methods for RCA.
Eight RCA methods, such as fishbone diagrams and 5 whys method, were compared to find the most suitable analytical method in the GCP area. A specific method for performing RCA and planning CAPA in the processes for issue resolution that includes understanding of the fact, determination of the root cause and planning of measures, was proposed by combining multiple analytical methods. The working group members were then divided into small groups to perform RCA on assumed cases using the proposed method. The result suggested that almost similar root causes were derived, although there were some differences due to different position of each member (sponsor or contract research organization [CRO], audit department or study operating functions), and that the method was useful and easy to use regardless of what degree of experience the RC analyst has.

The CAPA Examination Case Development Working Group collected issues from participating members, performed RCA by using 5 whys method and compiled examination cases where CAPA was developed.
A deliverable contains 13 cases that include all processes, results in the 5 whys method and developed CAPA, as well as the approach taken by this group, and Ten Ground Rules applied for RCA investigation.
This group realized that appropriate RCA could identify root causes of issues and result in the establishment of effective measures to resolve issues and we could get better RCA skills from a lot of experiences in case examination.

The Enlightenment Working Group has worked on discussion of CAPA with attention to implementation of the quality management system (QMS), because the revision of the “Guidance for the ‘Ministerial Ordinance on Good Clinical Practice for Drugs’” and the director’s notification of the “Basic Concepts Relating to Clinical Trial Quality Management” were issued simultaneously and adaption for the QMS was required. Some companies have already implemented their own QMS, whereas other companies need to establish the QMS including

preparation of standard operating procedures from now. The QMS must be understood by not only study operating functions but also management executives in the company. In consideration of the current situation, this group developed materials to help every company establish and operate their QMS. This group also prepared enlightenment materials to be used for the purpose of education after great deal of discussion based on the proposal within the group.

As subgroup of C3A, the Educational Joint Working Group, was established to work with CT2 that planned RCA/CAPA-related GCP Education Support Course and offered to collaborate. Some of the members were nominated themselves and participated in the organization of the course.
CT2 was responsible for the course operation and the lecture on the introduction to QMS, while this group was responsible for the planning of case scenario exercise, lectures on RCA/CAPA process, and instruction of exercise method. Two cases are used in the group work exercise. The course focused on RCA investigation because it was supposed that CAPA was relatively easy to determine if the root cause of issues could be found.
The deliverable includes the contents of the course, slides prepared by our working group, and knowledge from the course, which can be used for RCA exercises in each company.

Each subgroup explored different themes and thus our group could report four types of deliverables, which is considered to contain a lot of useful information to be used for reference by users.
The deliverable introduces many examination cases and RCA methods, which are results from investigations in each working group, as described above. However, they are just examples and we would like to ask each company to adjust them according to the situation at each company but not to use the information directly.

GCP Division, Activity Summary of the 14th Term (April 2018– March 2020)	
Study Group	**Study Group 3: Reliability Assurance**
Subgroup	**C-3-B**
Theme	**Risk-based quality control at study sites**

[Background and objective]
Many global studies have been recently conducted, and quality control is required in clinical studies in accordance with ICH-E6(R2). To assure acceptable quality in FDA or EMA's inspections, risk-based quality control is also important at study sites.
Subgroup A of Study Group 4, the predecessor of our group, developed a learning tool for providing a general workflow, extracting risks, and considering measures to reduce the risks during each process of clinical studies, "Risk-based Quality Management Toward Implementation of Risk Based Approach (RBA) in Medical Institutions," (hereinafter referred to as the "Learning tool") in March 2018, and released it on the JSQA's website. However, only releasing the tool was not enough for wide dissemination and could not be a trigger for site staff to use it. Continuing from the previous term, we therefore considered the contents of the Learning tool and the method for using it to further promote the use of the tool, which was determined to be the theme in the present term.

[Methods]
To examine the usability of the current version of the Learning tool, we conducted a web-based questionnaire survey among clinical research coordinators (CRC) via the large clinical trial network and the industry association of site management organizations (SMOs) between December 2018 and March 2019.
We also held a workshop using the Learning tool at a medical institution (university hospital in Tokyo). Before this workshop, we prepared materials for learning basic knowledge of risk-based quality control. During the workshop, the materials were distributed and used for simulation of identification of risks in clinical trial duties at medical institutions, investigation of the causes, and proposal of preventive measures. We also collected the information on methods for effectively using the Learning tool.

[Results and discussion]
Among 747 people who provided effective answers to the questionnaire, approximately 76% answered that they "just skimmed" it. We thus considered it necessary to add an easy explanation on expected effects and advantages of the Learning tool and make efforts to attract their attention. We also received an opinion that the tool was useful but it was difficult to understand how to use the tool.
In the workshop with CRC, we presented examples of the methods for using the tool, resulting in smooth group learning. Furthermore, we recognized the differences in thinking and perception among staff members (resulting in the coordination of perceptions) and confirmed that the Learning tool is also useful for experts and education officers.
Based on the results, we made a poster presentation to promote the Learning tool in the "19th Conference on the roles of CRC and clinical studies" in FY2019.
We also added an explanation on the method for using the tool and the need for process and risk control such that CRC and site staff members can learn the need for RBA by themselves.
A new version of the Learning tool will be released on the JSQA's website (for the public) in March 2020, as well as on the e-Training Center of the Center for Clinical Trials, Japan Medical Association, in collaboration of the Special Project Group 4.

GCP Division, Activity Summary of the 14th Term (April 2018–March 2020)	
Study Group	**Study Group 3: Quality Assurance**
Subgroup	**C-3-C**
Theme	**Investigation of audit methods for clinical research**

The Clinical Trials Act was promulgated on April 14, 2017, and the Ordinance for Enforcement of the Clinical Trials Act (ordinance by the Ministry of Health, Labour and Welfare) on February 28, 2018, and the related notifications were then issued by division and bureau directors to supplement Ordinance for Enforcement. Both the Clinical Trials Act and the Ordinance for Enforcement of the Clinical Trials Act came into effect on April 1, 2018. Under the situation where a trend in clinical research was attracting much attention of the industry, we started group activities.

To deeply understand the provisions of the Clinical Trials Act, the Ordinance for Enforcement of the Clinical Trials Act, and the related notifications, each member first investigated the interpretation of provisions to develop detailed explanatory materials and shared the results of the investigation.

To examine audit methods based on the Clinical Trials Act, we prepared the flow chart of conducting a clinical research. Via the flow chart, we confirmed necessary procedures and documents for a specified clinical research from preparation to the completion. In preparing the flow chart of a clinical research, the following design was assumed:

- Study design: multicenter, double-blind, parallel-group study.
- Off-label use of an approved drug.
- The principle investigator has been selected by the sponsor.
- Medical writing, study site selection, monitoring, data management (DM), and statistical analysis are outsourced to a contract research organization (CRO) (selected by the sponsor and referred to the principle investigator).

Based on the flow chart of conducting a clinical research, we then prepared an audit checklist for a clinical research.

To prepare the checklist, we determined items to be checked in audits according to the following processes during a specified clinical research, in reference to the provisions, designated formats, the common format in the Clinical Trials Act, the Ordinance for Enforcement of the Clinical Trials Act, and the related notifications:

1) Before the start of a clinical research (from protocol preparation to jRCT registration)
   Requirements of the protocol and informed consent form are listed in a separate sheet.
2) During a clinical research (from jRCT registration to data lock)
3) At the time of study completion
   - ✓ From data lock to study completion: cases when a report of the primary endpoint is prepared.
   - ✓ From data lock to study completion: cases when no report of the primary endpoint is prepared.
   - ✓ From the decision of study discontinuation to study completion; discontinuation of the clinical research

Each item in the checklist was linked to the supporting provisions of the Clinical Trials Act, the Ordinance for Enforcement of the Clinical Trials Act, and the related notifications if possible.

[Discussion]

1. During the process for preparing the audit checklist based on the Clinical Trials Act, we understood the Clinical Trials Act, current complicated rules, and acquired knowledge necessary for conducting audits of clinical researches.
2. We will have to blush-up the audit checklist based on the Clinical Trials Act by using it at actual cases to increase its versatility.

GCP Division, Activity Summary of the 14th Term (April 2018–March 2020)	
Study Group	**Special Project Group 1**
Subgroup	**C-T-1**
Theme	**Examination of Case Examples of Compliance Reviews/Inspection**

Special Project Group 1 collected, examined, and analyzed 118 PMDA compliance reviews from Japan and overseas contributed by members of the JSQA GCP Division, and some 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 the inspection(s) by overseas regulatory authority reported from JSQA member, as well as relevant regulatory information mainly from public sources. We presented our results as feedback to the personnel who is the member of JSQA membership company at the annual event, "What's Quality & Compliance? – Review Meeting on Case Examples of Compliance Reviews/Inspections –."

1) Conferences

(1) What's Quality & Compliance? – 39th Review Meeting on Case Examples of GCP Compliance Reviews/Inspections –

・39th Meeting: March 08, 2019, Nissho Hall, Tokyo (attendance: 614)

- Basic Course: Presentation about "Compliance Review & GCP inspection conducted by PMDA" that is available on the JSQA website
- Basic Course: CAPA & RBA (introductory session about Corrective Action and Preventive Action (CAPA) & Risk Based Approach (RBA) updated with revised deliberation results presented in the previous 37th and 38th Review Meetings
- Trends in inspections by overseas regulatory authorities (including presentation by Special Project Group 5 on GCP inspections by Chinese regulatory authority)
- Case examples of compliance reviews by PMDA (including the results of deliberations by Special Project Group 1)
- Panel Discussion on Good clinical study management based on the consideration of case examples provided in the previous "Case examples of compliance reviews by PMDA" session with invited panelists (a Hospital Pharmacist and a CRC of SMO) and Special Project Group 1 members

(2) What's Quality & Compliance? – 40th Review Meeting on Case Examples of GCP Compliance Reviews/Inspections –

・The 40th Meeting scheduled for March 06, 2020 (Nissho Hall, Tokyo) was cancelled on February 19, 2020 due to the outbreak of coronavirus across Japan. Followings were planned topics for the 40th Meeting.

- Trends in inspections by overseas regulatory authorities (including presentation by Special Project Group 5 about feedback from 6th GQAC conference held in February 2020)

- Invited lecture: Experience with EMA and US FDA inspections in Japan
- Case examples of compliance reviews by PMDA (including the results of deliberations by Special Project Group 1)
- Panel Discussion on Good clinical study management based on the consideration of case examples provided in the previous “Case examples of compliance reviews by PMDA” session, with invited panelists (a Hospital Pharmacist and a Clinical Trial officer of SMO) and Special Project Group 1 members

2）Deliverables

- Summary of deliberation results (39th Meeting) [distributed to Meeting participants and to companies which contributed case examples]
- Summary of deliberation results (40th Meeting) [(Planned action) It will be released on the JSQA website but only accessible to GCP Division members]
- GCP compliance review reports (39th Meeting) [released on the JSQA website but only accessible to GCP Division members who participated in the Meeting and to companies which contributed case examples]
- GCP compliance review reports (40th Meeting) [(Planned action) It will be released on the JSQA website but only accessible to GCP Division members]
- Data Listing of case examples of compliance reviews collected using the Law Concerning Access to Information Held by Administrative Organs [released on the JSQA website accessible to all JSQA members]

GCP Division, Activity Summary of the 14th Term (April 2018 – March 2020)	
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**

We held 5 types of GCP training courses for personnel in charge of clinical trials. The courses ran for a total of 6 sessions over a term of 2 years.
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.
Through the participation in course development, the members of Special Project Group 2 were able to deepen their knowledge and understanding of GCP quality control, audits, and quality assurance, and resulted in upgrade their own skills.
In this term, Special Project Group 2 members met once monthly in general for a total of 23 meetings for the purpose of course development.

The followings are overviews of courses which we conducted.

QC/QA Beginners' Course (Offered twice: July 2018 and July 2019)
One-day course, Participants: 99 people in July 2018 and 88 people in July 2019
This course was offered to new staff of 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 the following 4 lectures: "Overview of the Pharmaceutical Affairs Law and GCP", "Post-marketing regulation and its recent topics", "Features and practicalities of clinical trials for medical device" and "Overview of QC/QA".

Basic Course for Auditing to Investigator / Institution (Offered once: February 2019)
Two-day course, Participants: 36 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 acquiring and/or upgrading the skills necessary for auditing clinical trial sites. Through review of essential documents and source data, and interview with site staff, participant learned how to proceed with auditing and the process of identification of findings and also, they realized that there were various viewpoints and ways of thinking from group discussion.
It was a feature that participants were able to do interviews with real medical institution personnel with clinical trial experience with the cooperation of Hamamatsu Medical University.

Basic Training Course for Quality of Clinical Study (Offered once: September 2019)
One-day course, Participants: 34 people
This course was offered to persons with 6 months to 1 years of experience in GCP QC or monitoring operations. The sessions featured a lecture titled "Practice and Overview of Quality Control" and group discussions of case study exercises focused on quality control operations for "clinical trial documents etc.

Basic Training Course for CAPA based on Root Cause Analysis (Offered once: December 2019)
One-day course, Participants: 35 people
This course was offered to those who learned about Root Cause Analysis (RCA) for the first

time or wanted to check the basics. It consisted of the lecture of QMS overview and followed by case study exercises in order to better understand RCA.
This course was conducted in collaboration with Study Group 3-A, GCP division.

GCP Audit – Basic Training Course (Offered once: January 2020)
One-day course, Participants: 42 people
This course was offered to persons with less than 3 years' experience in GCP audit operations, and consisted of the following 2 lectures: "Introduction to GCP audit" and "more detailed process of GCP audit from planning to reporting of audit report was included", followed by case study exercise to understand general audit process and the point of interest of investigator site audit.

GCP Division, Activity Summary of the 14th Term (April 2018–March 2020)	
Subcommittee	**Special project Group 3**
Group	**C-T-3**
Theme	**Submission of public comments, dissemination of amendments to GCP, etc.**

1. Response to public comments

For the following guidelines (draft) in which opinions were invited, the opinions to be submitted were reviewed from the perspective of JSQA and submitted to MHLW.

- ICH E19 Guidelines on Optimization of Safety Data Collection (draft)
- ICH E8 (R1) Guidelines on General Considerations for Clinical Studies (draft)
- Ordinance for Enforcement of the Clinical trials Act (draft)

Authority responses to the following public comments submitted in the previous period were summarized and posted on the JSQA public HPs:

- ICH E17 General principles for planning and design of Multi-Regional Clinical Trials (draft)
- Guidance for partial revision of "Guidance on the Standards for the Implementation of Clinical Studies of pharmaceuticals" (new and old comparison table) and "Fundamental Concepts for risk-based monitoring" (draft)

2. Dissemination of the content of amendments to the GCP

In order to facilitate understanding of the changes in the revision, the following documents were created and released to the JSQA public HP (*Joint work with Japan Association of the Clinical Study Textbook).

- Revisions to "Guidance for Ministerial Ordinance on Good Clinical Practice for Drugs" in a comparative edition of the prior and amended article provisions*
- Training materials on the above-mentioned materials*
- Changes to clinical trial documents or records (dated July 5, 2019) from the previous notification (a comparative edition of the perior and amended descriptions)

3. General comments and discussions

- The items described in the activity summary could be rapidly treated, and the quality of the deliverable was satisfactory.
- As results of the questionnaire conducted relevant to the activity 1 "Response to public comments", approximately 70% of respondents were affirmative to this activity, and it was considered that the continuation of this activity would be meaningful even in the future.

GCP Division, Activity Summary of the 14th Term (April 2018– March 2020)	
Study Group	**Special Project Group 4**
Subgroup	**C-T-4**
Theme	**Participation in planning of external joint seminars**

After beginning its activities under the theme above in 2013, Subgroup C-T-4 conducted the following activities in the present 4th term:

1. Planning and holding of JSQA-organized external seminars

"What is a 'proper record'? -Let's think together- ," a seminar in the 18th Conference on CRC and Clinical Trials 2018 in Toyama

"Why does an auditor request us to store even 'sticky notes'?", a seminar in the 19th Conference on CRC and Clinical Trials 2019 in Yokohama

We conducted lectures and group discussions (in which some members of Subgroup C-3-B participated) in the 18th Discussion Meeting on Trial Duties (the Tokyo Metropolitan Society of Health System Pharmacists).

We participated in the eTraining Center, which was organized by the Japan Medical Association, as a subcommittee member and provided teaching materials: "Risk-based quality control for implementing the Risk-Based Approach (RBA) at medical institutions (revised C-3-B non-routine deliverables)" and "What is a 'proper record'? (revised materials for the 18th Conference on CRC and Clinical Trials)."

We did not plan any seminars in the meeting of the Japanese Society of Clinical Pharmacology and Therapeutics because the theme did not correspond to the JSQA's activities last year and the schedule was similar to that of the Conference on CRC and Clinical Trials in this fiscal year.

2. Management of lecture requests

• Regarding the procedures and management according to the "Approval of lectures presented by the GCP Division" (GCP Division Internal Rule 01 Ver. 2.0), no documents were submitted by other subgroups.

• We will continue to consider methods for requesting lectures presented by the GCP Division.

GCP Division, Activity Summary of the 14th Term (April 2018– March 2020)	
Study Group	**Special Project 5**
Subgroup	**C-T-5**
Theme	**Promotion of globalization in reliability assurance service**

Special Project 5 continued the activities in the previous term, discussed common issues, and did the following activities in three teams (EU/USA team, Chinese team, and South Korean team).

- Common issue: Discussion on cultivating communication with external QA organizations (such as RQA/SQA), discussion on planning of the 6th GQAC oral session, and presentation in the conference of GCP compliance review/inspection cases held by Special Project 1
- EU/USA team: Discussion on pharmaceutical-related regulations, details of GCP inspection-related notifications, etc., of the FDA/EMA/MHRA
- Chinese team: Discussion on pharmaceutical-related regulations, details of clinical trial- and GCP inspection-related notifications, etc., in China
- South Korean team: Discussion on pharmaceutical-related regulations, details of clinical trial- and GCP inspection-related notifications, etc., in South Korea

After the activities, the subgroup

- could cultivate communication with the GCP-related activity group in the external QA organizations (such as RQA/SQA) and hold the 6th GQAC oral session as a joint project;
- presented the latest relative regulations and GCP inspection trend in China in the conference of GCP compliance review/inspection cases held by Special Project 1 (March 2019); and
- could gather information on relative regulations and notifications in the EU/USA, China, and South Korea continuously; summarize and make lists of important notifications; and issue a work product to support promotion of globalization in reliability assurance services of the member companies.

It was planned that the activity would be done by the “Study Group” in the next term.

GCP Division, Activity Summary of the 14th Term (April 2018– March 2020)	
Study Group	**Special Project Group 6**
Subgroup	**C-T-6**
Theme	**Q&A for GCP Quality Management and Quality Assurance Managers**

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.

In the previous (11^{th}-13^{rd}) term, Special Project Group 9 ,Subgroup C-2-C and last Special Project Group 6 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. Special Project Group 6 continued the 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 ,Subgroup C-2-C and last Special Project Group 6. For better convenience when searching for relevant cases, the Q&A compilation features a listing categorized by GCP provisions, plus an added search function.