Activity Summary of the 12th Term (April 2014 – March 2016)	
Study Group	**Joint Special Project Group 1**
Subgroup	**K-T-1**
Theme	**Quality assurance relating to GMP and CMC**

Joint Special Project 1 was set up in April 2006 as a cross-working group activity of the Japan Society of Quality Assurance (JSQA), to examine what quality assurance relating to GMP and CMC should be from a wide perspective.

In the previous term (4th term, Year 2012 - Year 2013), the 4 themes of "Examination of case examples to solve various questions pertinent to GMP for Investigational Medicinal Products/GMP for Drug Products <Group A>," "Examination of issues to operate ICH Q10 <Group B>," "Examination of GMP-related education and training <Group C>," and "Investigation of Q&A of PIC/S GMP Guide (the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme Guide to GMP) <Group D>," were discussed under the group task of "Examination of what quality assurance relating to GMP and CMC should be," and the results were compiled as deliverables. Group B also presented the results of their research at the 4th global QA Conference that was held in the US in April 2014.

In this term (5th term, Year 2014 - Year 2015), we discussed 4 themes based on the key words of "PIC/S," "Quality Culture," "QRM," and "inspections," under the group task of "Examination of what quality assurance relating to GMP and CMC should be," and compiled the results as the deliverables. In the field of GMP/CMC, Japan was approved as a member of PIC/S in July 2014, and it is expected that an increasingly global approach will be followed. Different companies are now engaged in finding ways to handle the so-called "6 gaps" challenges that were pointed out by the authorities. Against this background, there is a renewed focus on Quality Culture building, and there is a pressing need that a system based not only on Knowledge Management (KM), one of the methods of attaining ICH Q10 we have been working on, but also on Quality Risk Management (QRM: ICH Q9) will be entrenched in organizations. Each company is putting much energy into a better understanding of the regulations, the education of persons involved in GMP, and the necessary inspections and auditing for handling global studies, but it also means that the entire organization should realize the overall need for quality improvement activities.

During this term, approximately 40 members have participated in discussions on the timely theme of pharmaceutical industry guarantees, and members with a QA perspective could gain an even deeper understanding. Group activities were planned based on small group movement, and themes were basically decided through consensus among the members. At the end of the first and the second halves of the term, presentations on the 4 themes were held within the group. In the second half of the term, members also organized a mini lecture

meeting. All of these group activities have greatly contributed to members' understanding of the group themes and their enthusiastic participation.

In this way, the activities during this term provided opportunities for discussions and activities of an even wider range of themes than before. We believe that the group activities that have been built up by the Joint Special Project have thus advanced further. During the next term, we will continue to strive to enhance our group activities to achieve even higher quality and productivity.

Activity Summary of the 12th Term (April 2014 – March 2016)	
Study Group	**Joint Special Project Group 1**
Subgroup	**K-T-1**
Theme	**Discussion on the application of PIC/S GMP and PIC/S GDP to investigational medicinal products**

At present it is required for post-marketing drug product to comply with PIC/S GMP as the global standard. Japanese regulatory agency joined PIC/S in 2014 and amended a part of GMP regulation to bridge the gap between Japanese GMP and PIC/S GMP. . On the one hand, Investigational Product GMP is positioned under the GCP ordinance, not under the revised GMP in Japan. Therefore, there is small quantity of specific correspondence examples of the implementation between GMP and GCP, respectively.

Therefore, during the 12th term, we performed a questionnaire survey of KT1 participants' pharmaceutical companies to learn the present actual situation at the various pharmaceutical organizations concerning the activities for PIC/S GMP as pertaining to Investigational Products and to extract the precautions and challenges that will be helpful when promoting its introduction in the future.

We also discussed information concerning GDP obtained from the results of the questionnaire survey.

Activity Summary of the 12th Term (April 2014 – March 2016)	
Study Group	**Joint Special Project Group 1**
Subgroup	**K-T-1**
Theme	**Quality Culture**

This group selected “Quality Culture” as a theme and has also been designated as “Quality Culture Team.”

What is Quality Culture?
ISO 9000 defines “Quality” as a “degree to which a set of inherent characteristics fulfils requirements”.

“Culture” is derived from the latin word “Colere” which has meaning more relevant to “cultivating a heart” or “developing a heart” in recent years.

That being said, good Quality Culture within a company means a process must exist to meet the customer’s requirements by taking the following steps: “nurture a heart” ⇨ “nurture an individual” ⇨ “nurture an organization” ⇨ “nurture a company” ⇨ “nurture a company culture”, and finally, “being able to nurture a system that assures high quality.”

In conclusion, we believe it would be beneficial to research what is required to develop a good Quality Culture and/or ingrain this into our organization. Therefore, we selected “Quality Culture” as our theme of study.

Activity Summary of the 12th Term (April 2014 – March 2016)	
Study Group	**Joint Special Project Group 1**
Subgroup	**K-T-1**
Theme	**Understanding and practices of the Quality Risk Management throughout the life cycle of drugs**

The International Council on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), adopted the Step 4 guideline ICH Q9 "Quality Risk Management" (QRM) on November 9, 2005. In Japan it was issued as the "Guidelines for Quality Risk Management" by the Director, Evaluation and Licensing Division, Compliance and Narcotics Division, Pharmaceutical and Food Safety Bureau (PFSB), Ministry of Labour, Health and Welfare (MLHW), and the Director, Compliance and Narcotics Division, PFSB, MLHW (PFSB/ELD No.0901004 and PFSB/CND No. 0901005) on September 1, 2006.
In this term, our goal was to understand QRM, and to practice to effectively apply QRM when actual problems, etc. occur, as well as when validating, etc.
This time, each company prepared mock-ups based on actual cases. Not only that it served good training to understand QRM better, but also it is expected that these mock-ups can be applied practically when taken back to the originated companies We considered that it would be useful to compile the questions, the key points and precautions pertaining to the practical application of QRM discussed during the preparation of the mock-ups as deliverables, so that others struggling with similar problems, misunderstandings, etc. can benefit from our studies.

At first there were very few of the member companies represented on our team that had already adopted QRM, and the degree of understanding of QRM also differed widely among the members. Companies that had already adopted QRM also still had many questions and problems with it, which shows that QRM is not fully implemented in those companies yet.
We realised that it was necessary to study the basics of QRM first, and as study materials, we read the "ICH Q9 Briefing Pack" that had been prepared as support materials by some members of the ICH Q9 Expert Working Group, especially the "Content" of the slides intended to provide an overall view. After we had obtained a certain degree of understanding, we started work on the preparation of mock-ups.
As we proceeded with the reading of the briefing pack, and also during the actual preparation of the mock-ups, various questions arose; for example, which of the formal flow or informal flow should be chosen when starting QRM, how corrective and preventive actions (CAPA) after deviations, etc., are different from the QRM, and how risk review and risk communication differ from each other. Our interpretations of these problems are explained in the next chapter, "Understanding QRM." Finally, the mock-ups that were prepared through this process as well as their background information were included in the deliverables. QRM

will become an important tool throughout the life cycle of drugs, and we discussed the key points and precautions of the QRM we have gained during preparation of these mock-ups.

Activity Summary of the 12th Term (April 2014 – March 2016)	
Study Group	**Joint Special Project Group 1**
Subgroup	**K-T-1**
Theme	**Preparations for inspections**

In the inspection team our goal was the appropriate and efficient inspection (audit) of each individual pharmaceutical company. We proceeded by investigating what kind of preparations would be useful from the respective viewpoints of the inspected (auditee) side and the inspector (auditor) side.

After Japan joined PIC/S in July 2014, inspectors (auditors) have been expected to adhere to PIC/S GMP level management. In reference to documents and Empirical knowledge, the inspection team therefore organized the points that the inspected (auditee) should keep in mind when preparing for inspections (audits) with the goal of having efficient and smooth inspections (audits).

In August 2013, the enforcement notification of PIC/S was issued, and “Starting and packaging materials supplier management” became a requirement, but until now, there have been frequent cases where inspections of the active pharmaceutical ingredient makers have mainly been performed, but inspection of the Starting and packaging materials has not been considered very important. Therefore this inspection team organized the points that the inspector should keep in mind when preparing for inspections (audits) with the goal of performing appropriate and efficient inspections.

We will be pleased if the use of the deliverables will benefit future inspections (audits).

Activity Summary of the 12th Term (April 2014 – March 2016)	
Study Group	**Joint Special Project Group 2**
Subgroup	**K-T-2**
Theme	**QA Methodology at Clinical/Medical Laboratories for Clinical Trials** －Examination of Problems with GCLP in Auditing－

Quality assurance of contract laboratories including central laboratories, pharmacogenetic laboratories conducting analysis of clinical samples (Good Clinical Laboratory Practice; GCLP) has attracted attention in the US and Europe, and JSQA has also been working on this topic as a Common Special Project since 2008. Due to the recent revision of the regulations (GCP Ordinance, guidance, etc.), the quality assurance of analyses of samples from clinical trials and storage of records have been reinforced and the related investigator sites (trial facilities), sponsors, etc. are working to respond to these changes.

Then, as the tasks of Joint Special Project Group 2 for this term, we discussed the problems on GCLP, and also, in view of recent environmental changes, set the specific themes for our activities as listed below, and worked on each theme.

Through this project, we have been attempting to present specific case examples by using questionnaires, and are working on the above tasks so that our work outcomes can be helpful for individual audit activities.

We hope that our work outcomes will also contribute to JSQA members' daily audit activities.

Group 1: Review of GCLP-related problems.
Group 2: Analysis of the current situation and issues for the precision management of the equipment for clinical trials.
Group 3: QA Methodology at Bioanalysis.
Group 4: History Background and Future Prospect in GCLP.
Group 5: Review of Draft Guidance for the Audit of a Clinical/Medical Laboratory.
Group 6: Preparation of a Poster Session in the 14th Conference on CRC (Clinical Reserch Coordinator) and Clinical Trials in 2014, based on the review of GCLP-related problems.
Group 7: Audit Perspective for Bioanalysis Assay.

Activity Summary of the 12th Term (April 2014 – March 2016)	
Study Group	**Joint Special Project Group 3**
Subgroup	**K-T-3**
Theme	**Issues for Regenerative Medicines**

In relation to regenerative medicines, the dedicated regulations for them were put into force in November 2014 and have continuously been legislated in Japan. The following activities were conducted in the12th term;

1. Investigated and discussed the related regulations and guidelines on the course of the research/development/post marketing of regenerative medicines, summarized them and published the summary documents on the JSQA web site.

2. Investigated and discussed NDA documents of the regenerative medicines that were submitted to MHLW, or were under development, summarized them and published the summary document on the JSQA web site.

Based on the activities for 2 years, it was agreed that there were no differences in terms of QA between regenerative medicines, medicines and medical devices. However, the CMC was the most important point in terms of the safeguarding of patients. CMC requirements of regenerative medicines can not be standardized.