GMP Committee for Sterile Products
January 2021
Chairperson, Yasuto Ikematsu, Osaka University
Vice-chairperson, Satoshi Sugimoto, Takeda Pharmaceutical Company Limited.
Vice-chairperson, Junko Ina, IBM Japan Inc.

This committee has the largest number of participants and has been active since 2004. The research is actively conducted either bimonthly and as needed within the 6 research groups and 1 subcommittee which has 3 research groups.

1 Group: Container Closure Integrity research
For sterile products, qualification of the barrier function for microorganisms needs to be demonstrated throughout their life cycle, and control of container closure integrity is one of the critical control elements. In recent years, the USP <1207>, which describes the concept of container closure integrity and management methods for sterile products, has been revised. In the JP 17 revision, the requirement for the barrier function of packaging is specified in the "General Notices for Packaging of Preparations". Thus, the requirement for the management of container closure integrity of parenteral preparations is increasingly being enhanced. However, the same test can't be applied to all products for the tests to assure the barrier properties, and among many test methods, an appropriate test method suitable for the product characteristics needs to be selected from the viewpoints of feasibility and reliability. In this group, factors that impair container closure integrity and their effects on contamination risk are sorted out, and the ideal way of container closure integrity test as a risk assessment method is examined.

2 Group: Injectable foreign matter visual inspection research
This group has been conducting research on insoluble foreign matter in injectable drug with the aim of standardizing the assurance method to meet the quality requirements in the Japanese market and eventually spreading it internationally. As the background, although the inspection methods for foreign matter have been harmonized among the Japanese Pharmacopoeia, the European Pharmacopoeia, and the United States Pharmacopoeia, the standard for foreign matter to be removed is still ambiguous: "Insoluble foreign matter that can be easily detected must not be accepted."

In Japan, the quality requirements for foreign matter in injectable drug tend to be higher than those in other countries, and therefore, additional visual inspection must be performed in Japan for products manufactured at overseas manufacturing sites. We are currently considering quantifying the detection ability of visual inspectors and standardizing the assessment method. If we can establish a quality assurance procedure with standardized level of inspectors, we will be able to be explain the objective qualification of the visual detectability objectively against the ambiguous criteria of "easily detectable insoluble foreign matter" required by the Japanese Pharmacopoeia, and it will be easier to achieve the quality required by the Japanese market internationally even in foreign manufacturing sites.

3 Group: Rapid microbiological method research

Microbiological quality control and environmental monitoring in the manufacturing process are important for manufacturing facilities of pharmaceuticals, human cell therapy and gene therapy products, and it is necessary to minimize the risk of microbiological contamination of products and to monitor their environment and quality.

In recent years, the value of rapid microbiological methods has been rapidly recognized, and the frequency of their inclusion in guidelines such as the 17th Edition of the Japanese Pharmacopoeia Reference Information and PIC/S (EU) GMP Annex 1 has increased. Therefore, the objective of this group is to contribute to the creation of new value in microbiological control for regulatory authorities, pharmaceutical companies, and suppliers by researching the concept and application of rapid microbiological methods and continuously publishing the results. In addition, the group consists of users (pharmaceutical company) and suppliers (equipment supplier), and conducts research that can be applied in a flexible manner, emphasizing practical implementation and qualification at manufacturing sites, etc. through approaches from both sides.

5 Group: Study of New Sterility Assurance and Contamination Control Strategy

In recent years, aseptic pharmaceutical production sites have been equipped with state of the art technologies that enable advanced aseptic environment control, such as isolators and RABS, and the practical use of fully automated aseptic grooveless isolators without human intervention is just around the corner. While progress has been made in aseptic pharmaceutical manufacturing technology, the

laws, regulations and guidance related to aseptic pharmaceutical manufacturing are still based on the conventional cleanroom manufacturing method, and GAPs are emerging. In this group, we are conducting research on the review and optimization of aseptic assurance and contamination control strategies for pharmaceutical manufacturing based on science based and risk assessment methods in response to the development of advanced aseptic environment control technologies. In addition, to discuss the contamination control strategies, we are investigating and organizing the historical background and significance of each technology and test method related to sterility assurance to deepen our understanding. Our group has made many contributions to Pharmatech Japan (magazine), and we have many opportunities to present our opinions.

6 Group: Containment Technologies Research

There are increasing opportunities to manufacture products with high pharmacological activity (highly active drugs) such as anticancer agents in respect of pharmaceutical manufacturing. There is also a growing demand for containment technologies to deal with chemical hazards and biohazards for production of vaccines which have been attracting attention in recent years, and for regenerative medicinal products in the manufacture of gene therapy products such as viral vectors or cell processing products with genetical modifications. It is desirable that such containment measures enable to take reasonable correspondence procedures suitably after evaluating impacts on products to be handled or workers within the facility by classifying the target hazard and the risk. This group sorts out the impacts of objects that require containment on other products and workers, and discusses the appropriate design for premises and equipment and its operation corresponding to the hazard and risk. The group also discusses the technical issues on achieving both hazard control and aseptic manufacturing.

7 Group: PIC/S GMP Annex 1 Study

Modern aseptic manufacturing has a wide range of expectations and demands for corporate practices, such as quality assurance of patient outcomes, active use of the latest technologies, QRM-based process understanding and rationale, and justification of control strategies based on design concepts and obtained data. The interest in EU-GMP _ Annex 1 as a defect standard to establish or continuously improve them is increasing every year. This group focuses on the changes from

the current version of Annex1 to the revised DRAFT (Version 2017, 2020) and on the unchanged philosophy.

Subcommittee on Good Gene, Cellular, and Tissue-based Products Manufacturing Practice (GCTP) for Human Cell Therapy and Gene Therapy Products

8 Group: Research on aseptic procedure
9 Group: Research on manufacturing process
10 Group: Research on regulatory science

Human cell therapy and gene therapy products are aseptic products and the requirements for their manufacturing and quality control are based on the GCTP. Compared to the manufacturing of pharmaceutical products, human cell therapy and gene therapy products are manufactured in smaller lots and require more human intervention, and more technical challenges for automation and mechanization, and thus relies on the manual skills of workers.
In addition, there are a wide variety of raw materials (Human cells) and final products, which often require case-by-case operation. Due to these circumstances, the industrialization of human cell therapy and gene therapy products is still its infancy, and there are many issues that differ from those of aseptic drug products, especially in the manufacturing and quality control of products. Our society believe that there is an urgent need for the development of technical know-how and regulatory science to discuss these issues and lead them to a global standard.
This subcommittee will address issues specific to human cell therapy and gene therapy products with “aseptic” as the keyword, and will establish three research groups (8 Group: Research on aseptic procedure, 9 Group: Research on manufacturing process, 10 Group: Research on regulatory science) to study the issues and solution faced in the manufacturing and quality control of these products.
The objective is to promote the revitalization and industrialization of the industry by conducting research on the issues and solutions facing the manufacturing and quality control of human cell therapy and gene therapy products and presenting the results to domestic and international audiences.

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