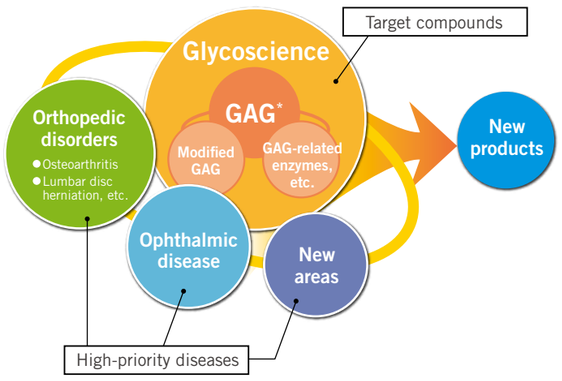
RESEARCH AND DEVELOPMENT

Seikagaku engages in research and development of innovative drugs in the our specialty field of glycoscience. And we contribute to the health and well-being of people around the world.

R&D policy

In order to rapidly and continuously create new products, Seikagaku engages in efficient R&D activities by focusing on target compounds and prioritizing target diseases. The focus of our drug discovery is glycosaminoglycans (GAG), which are the structural components known as glycoconjugates.

In research spanning nearly 70 years, we have accumulated a wealth of experience and expertise related to GAG drug discovery research and GAG production and formulation technologies. Today, we apply hyaluronic acid or unmodified GAG in pharmaceuticals and also engage in research and development of modified GAG produced using a cross-linking technology as well as enzymes and other substances that act on GAG. Given the properties of GAG, we focus mainly on orthopedic disorders and ophthalmic diseases as high-priority areas for now, where we have expertise through the development of such products as ARTZ Dispo joint function improving agent and OPEGAN ophthalmic viscoelastic device.



*GAG: Glycosaminoglycans
(One of the constituents of complex carbohydrates)

Direction of R&D and future drug discovery approach

Seikagaku possesses a GAG compound library, GAG-related enzymes, and wide-ranging technologies for manipulating these substances. We actively utilize these assets, accumulated in the course of research spanning many years, in drug discovery activities. We have also developed a global network of collaborating glycoscience researchers and engage in multiple joint research projects with universities and research institutes.

Specifically, we continue to focus on drug discovery for orthopedic disorders and ophthalmic diseases and have also begun utilizing GAG-related technology to expand new fields. At the same time, we make efforts to maximize the value of our products on the market or themes in development through expansion of indications, additional formulations, changes in dosage and administration, etc.

Until now, Seikagaku has followed a drug discovery approach of increasing the bioactivity of GAG, mainly through GAG modification and processing, and we are currently applying GAG to drug delivery systems (DDSs). Furthermore, going forward, we will also adopt an approach focused on the biological functions of sugar chains to open up new possibilities in drug discovery.

In our DDS, we are researching technologies that utilize the characteristics of modified GAG to freely control drug dose and the location and timing of release. We will pursue drug discovery and development capable of responding to a wide range of unmet medical needs by combining Seikagaku's DDS technologies with drugs and technologies that other companies possess, not only low-molecular compounds, but also proteins and middle molecules such as peptides and nucleic acids.

Seikagaku and glycoscience

Seikagaku's Management Creed states: "Under the principle of respect for learning, we contribute to human well-being by creating and supplying the world with safe and useful pharmaceutical products based on glycoscience." In keeping with this creed, we have made glycoscience the core foundation of our business and explicitly adopted a stance of respect for learning. Seikagaku's origin is closely bound up with this creed.

In 1950, Seikagaku became the first company in the world to successfully produce chondroitin sulfate, which is a sort of GAG, on a commercial scale. This breakthrough laid the foundation for our current business, which is centered on glycoscience. The manufacture of chondroitin sulfate marked the starting point for expansion of our business to bulk products, as well as reagents and diagnostics, and this has led to the strengthening of our ties to glycoscience-related academia and research institutes.

Through this close relationship with academia, we acquired the idea of applying hyaluronic acid in pharmaceuticals. R&D activities spanning many years culminated in 1987 with the successful development and launch of ARTZ, the world's first joint function improving agent whose main ingredient is hyaluronic acid. The development of HERNICORE, a treatment for lumbar disc herniation that contains condoliase, an enzyme that degrades GAG, also originated from collaboration with academia.

Seikagaku will continue to make glycoscience the central focus of R&D activities and, on the basis of research results in the field of glycoscience achieved in collaboration with universities and research institutes, strive to create pharmaceuticals and medical devices and deliver them to patients around the world.

The difficulty of applying glycoconjugates to pharmaceuticals

GAG are formed when amino sugars (sugars that include nitrogen atoms) and uronic acids (a class of sugar acids) or galactose are linked together to form chain-like structures (sugar chains). Sugar chains are known in the life sciences as the third biological chain, along with nucleic acids and proteins, but they have complex chemical structures because they are molecules that handle various kinds of information within living organisms. In research in areas such as structural analysis, automatic synthesis, and large-scale synthesis, this complexity poses characteristic difficulties not found in other biological materials.

However, long-term efforts in the industry and academia have advanced the structural analysis and synthesizing technologies of sugar chains. In addition, the genes of sugar-chain synthesizing enzymes and degrading enzymes have been comprehensively identified, and our understanding of the homeostasis of sugar chains in living organisms and their pathological function is advancing.

This progress in glycoscience technologies is closely linked with Seikagaku's drug discovery research.

Topics

The TATENO Forum contributes to enhancement of R&D capabilities

Each year in December, the Central Research Laboratory holds the TATENO Forum, an internal presentation forum for sharing research results relating to new ideas and technology creation. In addition to young and mid-career researchers, employees from other business sites participated, discussing the future potential and contribution to medical needs of each research theme.

In consideration of COVID-19, the forum for fiscal 2020 was held online for the first time, with 22 entries presented over a three-day period. At one point there were over 140 attendees, and by utilizing the advantages of holding it online, a lively discussion was had, with presenters answering questions from attendees via the chat function. Through the introduction of telework due to the effects of the COVID pandemic, many of the presented subjects showed ideas and approaches from new perspectives and points of attention.

We will continue to explore appropriate methods of holding future conferences as needed. By deepening interaction among employees through the exchange of ideas and information sharing as well as by contributing to the enhancement of Seikagaku's R&D and technological capabilities, the Central Research Laboratory aims to originate and create development themes, such as new pharmaceuticals that people truly need.

*The forum name was taken from the location of the Central Research Laboratory (Tateno, Higashiyamato City, Tokyo).

First online TATENO Forum

Research and development organization

To ensure close coordination of the drug development process from its upstream to downstream, Seikagaku has put in place an organizational structure in which the departments involved in R&D are consolidated under the control of the Research & Development Division. This integrated organization covers every R&D activity from clinical development to new drug application (NDA) and intellectual property strategy. In this structure, the Central Research Laboratory is in charge of exploring candidate substances and evaluating efficacy, safety, and pharmacokinetics, and the CMC Laboratory is responsible for production of investigational drugs, design of manufacturing processes, and consideration of commercial production.

Research & Development Division Structure

(As of April 1, 2021)

Drug discovery research

The Central Research Laboratory, Seikagaku's drug discovery research center, cultivates the creativity of researchers in a fulfilling research environment, equipped with advanced facilities, and places importance on fostering a self-help culture.

Seikagaku contributes unique knowledge, technology, and expertise related to glycoscience to benefit drug discovery research, and actively collaborates with universities and companies in Japan and overseas to accelerate the search for ideas and development of new technologies. Through these efforts, we work to create original pharmaceuticals and medical devices on the basis of specialized technologies and creative ideas.

[Overview of Research Units]

- Glycoscience: Exploration of GAG (glycosaminoglycans) and related compounds as pharmaceutical candidate substances
- Drug Discovery: Synthesis of new candidate substances with GAG as the basis for research, evaluation of their efficacy and function, and research on their actions and mechanisms
- Safety & Pharmacokinetics: Evaluation of pharmacokinetics and toxicity profiles of candidate substances in vivo
- Formulation Research: Exploratory research for the ascertaining and formulation of the physicochemical properties of GAG and GAG-related substances
- LAL Research: Development of manufacturing technologies for reagents and diagnostics based on exploratory research of new technologies

CMC research

The CMC Laboratory produces investigational drugs, designs manufacturing processes, engages in quality development, and examines commercial production of products under development created by the Central Research Laboratory. By engaging in development from the R&D stage in collaboration with the Production Division, the CMC Laboratory aims to ensure the stable supply of high-quality pharmaceuticals and medical devices that comply with regulations in Japan, the United States, and Europe and to increase the speed of new drug development under a system integrated from research to production.

[Overview of Research Units]

- Pharmaceutical Technology: Design of active pharmaceutical ingredients, pharmaceutical formulations, packaging, and manufacturing processes for candidate substances and consideration of commercial production
- Quality Development for CMC: Research of physicochemical properties, development of testing methods for quality evaluation, and quality assurance of investigational drugs

Intellectual property strategy

Appropriate protection of intellectual property relating to Seikagaku's technologies, products, and other assets is essential not only for maintaining corporate competitiveness, but also for continuing to create and supply unique, high-quality pharmaceuticals and medical devices. Seikagaku views intellectual property as an important management resource and engages in global intellectual property-related activities.

The Intellectual Property Department engages in activities related to acquisition of intellectual property rights (patents, designs, trademarks, copyright, know-how, etc.) and their protection. It works closely with the Research & Development Division involved in drug discovery as well as with Business Development & Marketing Division, Production Division, and other relevant Company organizations.

The clinical study process and paths of new drug development

To create new drugs, it is necessary to conduct various studies to evaluate efficacy and safety. Clinical studies are conducted to confirm whether drug candidates are actually beneficial to humans, following completion of research processes such as basic research and non-clinical studies.

Clinical studies are ordinarily divided into three phases and conducted at medical institutions such as hospitals in conformance with rigorous standards after the consent of subjects (healthy persons or patients) has been obtained.

A Phase I clinical study, the initial phase, is ordinarily conducted for the main purpose of examining the pharmacokinetics (absorption, distribution, metabolism, and excretion) and safety (adverse events and side effects) of investigational drugs in a small number of healthy subjects. A Phase II clinical study examines efficacy, safety, and pharmacokinetics and confirms optimal dosage and usage in a small number of patients. A Phase III clinical study, the final phase, objectively verifies efficacy and safety in comparison to existing approved drugs or placebos in large numbers of patients.

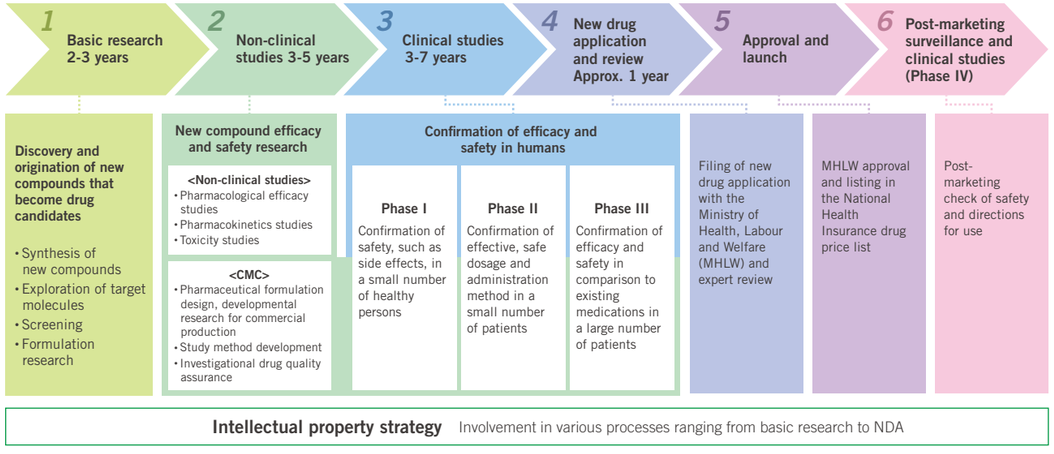
Ordinarily, more than ten years is required from discovery of a candidate substance until its approval as a new drug. Within the long, difficult new drug development process, clinical development is considered to hold the key to whether an NDA can be filed.

Clinical development

Seikagaku conducts various clinical studies in Japan and the U.S. in cooperation and collaboration with medical experts, medical institutions, and external contract research organizations (CROs) and site management organizations (SMOs). The Clinical Development Department is responsible for creating the integrated development plan (protocols); monitoring of clinical studies; planning and execution of enrollment acceleration; and data management and analysis of study results. It also communicates with the regulatory authorities in various countries and develops dossiers necessary at the time of NDA filing.

In developing protocols, the Clinical Development Department closely communicates with medical monitors and regulatory authorities, identifies requirements for NDA approval and finalizes the study design. In monitoring of clinical studies, the Department works through medical institutions to ensure the quality of studies by confirming whether they are being conducted in conformance with Good Clinical Practice (GCP) and regulatory requirements by ascertaining the condition of subjects and reviewing study data.

The Drug Research and Development Process



Ethical considerations concerning research using human biological materials

Progress in biological science has been accelerating in recent years, together with accompanying innovation of medical technologies. In particular, experiments and research using human biological materials, including genetic information, are yielding new knowledge that is expected to lead to the development of novel, highly beneficial pharmaceuticals.

In keeping with the intent of the Japanese government's guidelines on handling of human materials*, Seikagaku has established the Code of Ethics for Research Using Human Specimens to make it possible to conduct comprehensive reviews, including evaluation of ethical and scientific validity, when experiments and research using human materials are conducted. To carry out the intent of the Code of Ethics, we have established the Ethical Review Committee for Research Using Human Specimens and publish a list of committee members and minutes of committee meetings through the Japan Agency for Medical Research and Development's Ethical Review Committee Reporting System of the Ministry of Health, Labour and Welfare.

*Ethical Guidelines for Medical and Biological Research Involving Human Subjects (Only Japanese text available)

Ethical considerations in non-clinical studies

In the development of pharmaceuticals and medical devices, research activities using laboratory animals are indispensable to confirm the efficacy and safety of candidate substances, and deeply contribute to the progress and advancement of medical science.

Seikagaku strives to rigorously address ethical considerations in animal experiments and has formulated internal regulations that comply with the Act on Welfare and Management of Animals and Basic Guidelines for Animal Experimentation at Institutes under the Jurisdiction of the Ministry of Health, Labour and Welfare. Also, an ethics committee established within Seikagaku evaluates whether all animal experiments, including outsourced experiments, are planned and conducted in accordance with the 3Rs Principle*.These initiatives at Seikagaku have been evaluated as conformant by the Japan Pharmaceutical Information Center, a third-party organization.

*3Rs Principle: Methods that avoid or replace the use of animals (Replacement), methods that minimize the number of animals used per experiment (Reduction), and methods that minimize animal suffering (Refinement)

Development Pipeline

[Pharmaceuticals]

(As of September 30, 2021)

Development code, substance name		Indication	Developed in	Phase I	Phase II	Phase III	NDA
SI-6603	Condoliase	Lumbar disc herniation	USA			■	
SI-613	Hyaluronic Acid-Diclofenac Conjugates	Knee osteoarthritis	USA		■		
SI-613-ETP	Hyaluronic Acid-Diclofenac Conjugates	Enthesopathy	Japan		■ Late-stage Phase II		
SI-614	Modified Hyaluronate	Dry eye	USA			■ Phase II/III	
SI-722	Steroid conjugated with chondroitin sulfate	Interstitial cystitis and bladder pain syndrome	USA	■ Phase I/II			

[Medical Devices]

Development code, substance name		Description	Developed in	Pilot study	Pivotal study	NDA
SI-449	Cross-linked Chondroitin Sulfate	Adhesion barrier	Japan		■	

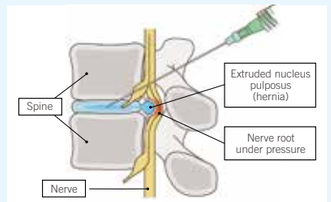
Overview of Development Pipeline

SI-6603 (treatment for lumbar disc herniation)

SI-6603, which contains condoliase as its active pharmaceutical ingredient, is a treatment for lumbar disc herniation directly injected into the intervertebral disc. It has the special characteristic of not requiring general anesthesia and being less invasive to patients than surgical treatment. Since a single injection is expected to improve the symptoms of lumbar disc herniation by reducing intervertebral disc pressure and relieving pressure on the nerve root, SI-6603 can contribute to improving patients' quality of life as a new treatment option.

In Japan, marketing approval was obtained from the Ministry of Health, Labour and Welfare in March 2018, and SI-6603 was launched on August 1, 2018 as HERNICORE 1.25 units for intradiscal injection.

In the U.S., although the expected pharmacological effect was demonstrated in a Phase III clinical study, the study did not meet its primary endpoint of improvement in leg pain. In response to this, we began an additional Phase III clinical study in February 2018, with a plan to complete follow-up observations in November 2022. However, the spread of COVID-19 infection has led to some medical institutions suspending clinical trials or halt hospital visits, which has caused delays in trial schedules. As of the end of March 2021, in addition to the operational status of trial facilities trending toward resuming their activities, promotion of subject enrollment has been successful, with enrollment making steady progress. We continue to seek to minimize delays, while also devising measures to reduce COVID-19 infection risk.



Administration of SI-6603

SI-613 (treatment for osteoarthritis)/SI-613-ETP (treatment for enthesopathy)

SI-613 is a formulation in which hyaluronic acid and diclofenac (an anti-inflammatory drug) are chemically bound using a drug binding technology proprietary to Seikagaku. By releasing diclofenac through hydrolysis, relief for osteoarthritis and enthesopathy can be expected.

In Japan, marketing approval was obtained for SI-613 for its efficacy and effect on osteoarthritis (knee joint and hip joint) on March 23, 2021, and it was launched as joint function improvement agent JOYCLU® 30mg Intra-articular Injection in May of the same year. It is the first joint function improving agent in Japan indicated for osteoarthritis.

In the U.S., a Phase II clinical study targeting osteoarthritis has been completed, and we are considering a Phase III study while proceeding with selection of a sales partner.

In April 2020, Seikagaku entered into an agreement with Eisai Co., Ltd. concerning co-development of SI-613 and a marketing alliance in China, and in September 2020, an agreement was made with that same company for a marketing alliance in South Korea.

Data analysis of a late-stage Phase II clinical study in Japan of SI-613-ETP for the treatment of enthesopathy has been completed, and we are considering the next clinical study together with co-development and marketing partner Ono Pharmaceutical Co., Ltd.

Administration of SI-613

SI-614 (treatment for dry eye)

SI-614, an ophthalmic solution, is a modified hyaluronate produced using Seikagaku's proprietary technology. Instilling this solution as an eyewash is expected to improve dry eye symptoms by protecting the ocular surface and promoting corneal wound healing.

In the U.S., a Phase II/III clinical study has been completed, and we are considering a Phase III study while proceeding with selection of a sales partner.

Administration of SI-614

SI-722 (treatment for interstitial cystitis and bladder pain syndrome)

SI-722 is a novel chemical compound in which a steroid is conjugated with chondroitin sulfate using Seikagaku's proprietary glycosaminoglycan modification technology and drug delivery systems. SI-722 injected into the bladder is thought to demonstrate an improvement effect in symptoms such as of frequent urination and bladder pain, by releasing a steroid with an anti-inflammatory effect.

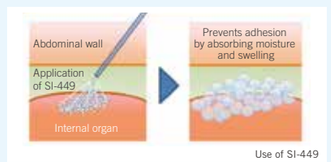
While a Phase I/II clinical trial in the U.S. experienced delays in the trial schedule due to the spread of COVID-19, subject enrollment was completed in January 2021, and tolerability in the patients of this trial has been confirmed. Currently, we are exploring the next phase of trials based on the data we have obtained.

Administration of SI-722

SI-449 (adhesion barrier)

SI-449 is a powdered adhesion barrier whose main ingredient is cross-linked chondroitin sulfate developed using Seikagaku's own glycosaminoglycan cross-linking technology. SI-449, which has the property of absorbing moisture and swelling, is expected to prevent or mitigate post-operative adhesion formation by forming a barrier between the surgical wound site and surrounding tissues after application. Development of this subject is progressing with an eye not only on domestic development, but also globally.

A pivotal study to confirm effect, safety, and operability was initiated in May 2020, but the trial schedule has experienced delays due to the spread of COVID-19 infections. We are currently exploring measures to make up these delays, such as expanding trial facilities, and are working remotely with facilities that have restricted visits.



Use of SI-449

PRODUCTION

Seikagaku steadily manufactures high-quality products at its two pharmaceutical manufacturing plants in Japan and endotoxin-detecting reagent manufacturing plant in the U.S. and plant related to CDMO business in Canada.

Production structure compliant with global standards

Companies that manufacture pharmaceuticals and medical devices must comply with the current regional regulations and engage in stable, continuous manufacturing. In order to deliver high-quality products to patients, Seikagaku complies with Good Manufacturing Practice (GMP) in Japan, the U.S., and Europe and strives for ever more rigorous manufacturing processes. Also, in the area of manufacturing control and quality control, we use computer systems to improve the completeness of records and are working to improve production efficiency through rigorous regular checks, elimination of human error, and improvement of manufacturing processes. We will continue to pursue continuous improvement and focus on the manufacture and supply of high-quality products that comply with global standards.

Ensuring a stable supply of products

Providing a stable supply of products is an important mission of a pharmaceutical company. Seikagaku prepares against major disasters and other risks by diversifying raw materials suppliers and maintaining appropriate inventory levels. At the Takahagi Plant, which is responsible for manufacturing the finished products, we have introduced a quake-absorbing structure that reduces shaking for the main production buildings when an earthquake occurs. Through these measures, we have put in place a system capable of stable, reliable product production even in an emergency.

Furthermore, to cope with product supply risk from distribution network disruption following a disaster, we maintain a certain level of product inventory and have pharmaceutical product warehouses in two separate locations: within the Takahagi Plant in Takahagi City, Ibaraki Prefecture in the Kanto region and in Hirakata City, Osaka in the Kansai region.

Environmental impact reduction initiatives

Seikagaku is keenly aware of the importance of protecting the global environment. We observe environment-related laws and regulations and voluntarily engage in environmentally friendly business activities. At our plants, in the treatment of water used in pharmaceutical production, we have introduced electro-deionization facilities that use no hydrochloric acid or caustic soda and, in wastewater treatment, we have adopted a system that uses ozone treatment and the activated sludge process.

Also, with the objective of reducing CO_2 emissions, we have established the Energy Conservation Promotion Committee and are managing energy use, and we are implementing improvement measures as well as providing education and training on energy conservation to achieve reduction targets set at each business site. Furthermore, the committee is putting in place a framework for increasing efficiency at the Group level by coordinating energy use and CO_2 emissions results and reduction measures for each fiscal year, reporting to the Management Committee, and deliberating on related matters. As a result, we have achieved our average energy reduction rate targets for the five years up to fiscal 2020.

Overview of Production Sites

Takahagi Plant (Takahagi City, Ibaraki Prefecture)

The Takahagi Plant, located in northern Ibaraki Prefecture, is responsible for manufacturing finished pharmaceuticals and medical devices, including the joint function improvement agents that are Seikagaku's mainstay products. When the plant opened in 1975, it had 28 employees. Since the launch of hyaluronic acid formulations in 1987, it has steadily expanded production scale as a manufacturing plant that specializes in injectable formulations. Today, the Takahagi Plant occupies a site of approximately 86,000 square meters and has five production buildings and some 200 employees.

The Takahagi Plant is one of the world's largest manufacturing sites for hyaluronic acid pre-filled syringe formulations*, producing more than 25 million units per year for the Japanese and overseas markets. Sterility assurance is strictly required for the manufacture of injectable formulations, and the plant has minimized the risk of contamination by implementing unattended, automated manufacturing processes. The plant possesses facilities and equipment that can be adapted to optimal sterilization methods suited to the product characteristics.

*A kit with an injectable syringe that has been filled with solution.

Kurihama Plant (Yokosuka City, Kanagawa Prefecture)

The Kurihama Plant, which manufactures bulk products, opened in 1947 and is Seikagaku's most experienced plant. The plant has some 100 employees and manufactures high-purity hyaluronic acid and chondroitin sulfate for use mainly as active pharmaceutical ingredients.

The most important characteristic of the Kurihama Plant is that it specializes in the manufacturing of bulk products by extraction and fermentation. The plant applies advanced chondroitin sulfate extraction and fermentation technologies nurtured over many years since the founding of Seikagaku and has expertise in the efficient manufacture of high-purity bulk products from chicken combs, the raw material of hyaluronic acid, and shark cartilage, the raw material of chondroitin sulfate.

The Kurihama Plant is also responsible for some of the manufacturing processes for condoliase, the active pharmaceutical ingredient of HERNICORE, a treatment for lumbar disc herniation. The plant is currently preparing to start up new bulk condoliase manufacturing facilities to further strengthen the production scale.

Information on U.S.-based Associates of Cape Cod, Inc. and Canada based Dalton Chemical Laboratories, Inc. is provided in the section "Overseas Subsidiaries" on page 50.

Topics

A robust and flexible organization: instilling a Quality Culture

Seikagaku's manufacturing department works to instill in the Company a Quality Culture, so it can be agile and flexible, maximally effective, and capable of reliably manufacturing high-quality pharmaceuticals.

As part of that, we have incorporated the Theory of Constraint (TOC), a philosophy of overall optimization, to develop our human resources to think and act autonomously. We implement a practical learning method greatly different from conventional training where an employee thinks of a subject on their own, takes action to present it, discusses it with everyone, and then considers the next steps.

By adding human resources that can think and act according to the foundation of improvement we have built so far, we encourage participation in activities that work to build an organization that continuously demonstrates high-quality workplace capabilities.

Practical learning for thought and action

MARKETING

Seikagaku has a unique business model of supplying products through external partnerships in Japan and overseas in collaboration with pharmaceuticals and medical device sales companies. In this way, it intends to focus and develop its business activities without having an in-house pharmaceuticals sales division.

Pharmaceuticals and medical devices

Seikagaku manufactures pharmaceuticals and medical devices with, as their main ingredient, glycosaminoglycans (GAG) such as hyaluronic acid, which are the structural components of glycoconjugates, and also products based on enzymes that act on GAG. To deliver these products to patients globally, Seikagaku forms partnerships with pharmaceutical companies that have expertise in each market, including Japan.

Through their activities, our partners, in conformance with laws and regulations on pharmaceutical sales, provide appropriate information on product efficacy, safety, quality, and other matters to physicians on a timely basis. Seikagaku, in close cooperation with sales partners, formulates sales strategies, supports preparation of product information materials, analyzes the market environment, including information on competing products, and collaborates with academic societies. Through these activities, we support sales partner activities and appropriately promote market penetration for our products.

As part of product life cycle management, Seikagaku is implementing product modifications that respond to needs of a changing market. One example is the conversion of the material for syringes, used for the joint function improving agent ARTZ Dispo, from glass to plastic. Through these efforts, we are adding value to our products.

Furthermore, we have been accelerating overseas business expansion in recent years. We are working to increase sales in countries where we already do business, and to meet global medical needs, we are implementing a plan to introduce existing products and products in development into new markets.

Bulk products

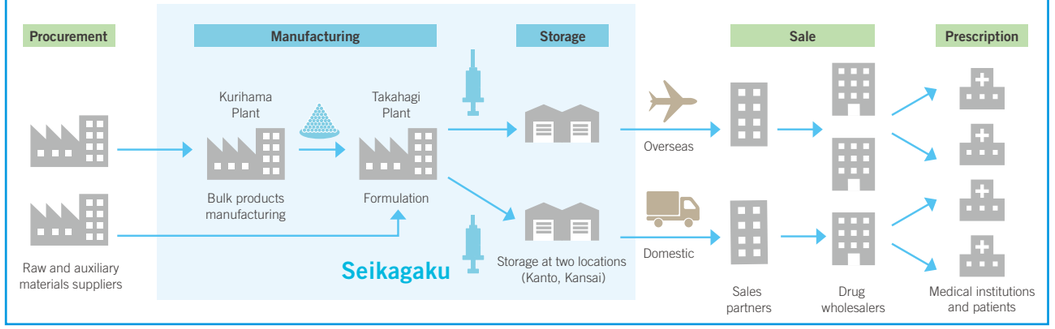
Using proprietary extraction and purification technologies, Seikagaku manufactures high-purity and high-quality hyaluronic acid and chondroitin sulfate and sells them to pharmaceutical and cosmetic companies, and others globally.

The bulk products are widely applied as active pharmaceutical ingredients for orthopedics and ophthalmology. In recent years, those bulk products are also being considered as new application materials in the regenerative medicine area.

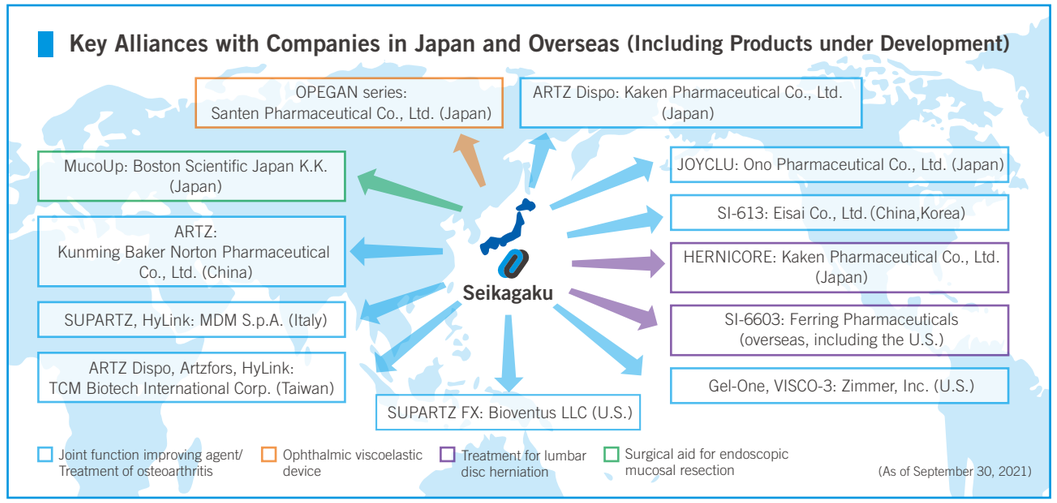
Contract development and manufacturing organization (CDMO)

A contract development and manufacturing organization (CDMO) is a business that supplies comprehensive services in drug development and manufacturing to pharmaceutical companies, including contract drug manufacturing, pharmaceutical formulation planning at the development stage, manufacturing of investigational drugs, and optimization of manufacturing conditions. In March 2020, we added to our business by acquiring Dalton Chemical Laboratories, Inc. as a subsidiary.

Supply Chain for Main Products



Key Alliances with Companies in Japan and Overseas (Including Products under Development)



LAL business

Seikagaku is engaged in the development of the LAL business in Japan, which is mainly used in quality control of injectable pharmaceuticals and medical device manufacturing processes and water quality control of dialysate used in artificial dialysis.

Wholly owned subsidiary Associates of Cape Cod, Inc. (ACC) handles overseas business development. ACC is the first company in the world to successfully develop endotoxin-detecting reagents from limulus amebocyte lysate (LAL), and it obtained U.S. Food and Drug Administration (FDA) approval in 1977. ACC plays an important role in the overseas business expansion through its global sales network, mainly in the U.S. and Europe, through the manufacturing and sales of endotoxin-detecting reagents, as well as beta-glucan-detecting in vitro reagent to diagnose invasive fungal disease.

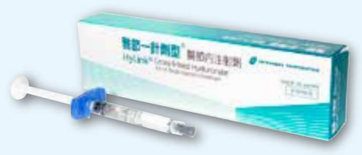
Topics

Launch of HyLink intra-articular single-injection joint function improving agent in Taiwan.

In August of 2021, Seikagaku began sales of HyLink in Taiwan.

HyLink is an intra-articular single-injection viscosupplement (a medical device for the treatment of knee osteoarthritis). Its main ingredient is a hyaluronate hydrogel created using Seikagaku's unique cross-linking technology. Since the highly viscoelastic hyaluronate hydrogel remains in the knee joint cavity for a long period of time, even administering only 3mL can be expected to provide a long-lasting improvement of symptoms.

Since the population is aging, the Taiwanese market for hyaluronic acid treatments is expected to grow. With the addition of HyLink to the multiple-injection joint function improving agents (ARTZ Dispo and Artzfors) that are already on the market, patients will be provided even more treatment options, contributing to improvements in their quality of life.



HyLink®

QUALITY COMPLIANCE

Seikagaku's mission is to provide patients with a continuous supply of safe, beneficial, high-quality pharmaceuticals and medical devices. We have constructed corporate quality assurance and compliance systems in accordance with laws, regulations, and standards.

Quality compliance system

Seikagaku makes maximum effort to ensure quality at every stage, from R&D to post-marketing, by complying with the pharmaceutical laws and regulations of overseas countries, including a collection of regulations and guidelines called GxP*. In Japan, as a marketing authorization holder, we have developed a system with three key roles (general marketing compliance officer, quality assurance supervisor, and safety management supervisor) and implement appropriate quality management and pharmacovigilance operations in accordance with the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices ("PMD Act").

To continue to reliably provide pharmaceuticals and medical devices required by patients around the world, we will strive to maintain and enhance quality assurance and compliance systems in accordance with global standards.

*GxP is an abbreviation for Good XXX Practice, a collective term for standards established to ensure the efficacy, safety, and quality of pharmaceuticals and medical devices from the R&D stage to post-marketing. (See the diagram to the right.)

Quality management system based on global standards

To provide a stable supply of high-quality pharmaceuticals and medical devices, in accordance with our Quality Policy, we have developed a world-class quality management system. At the development stage, we ensure reliability under Good Laboratory Practice (GLP) and Good Clinical Practice (GCP) standards. To ensure compliance with laws and regulations and maintenance of quality assurance systems through the post-marketing stage, each year we systematically conduct self-inspections and internal audits to confirm the status of operation of the quality management system and promptly take corrective and preventive actions as necessary.

Seikagaku has obtained ISO 13485 certification for the development, manufacture, and distribution of sodium hyaluronate-based viscoelastic products for the treatment of osteoarthritis of the knee and periarthritis of the shoulder. We strictly maintain and control quality at all stages from product design and development to post-marketing in conformance with these manufacturing control and quality assurance systems.

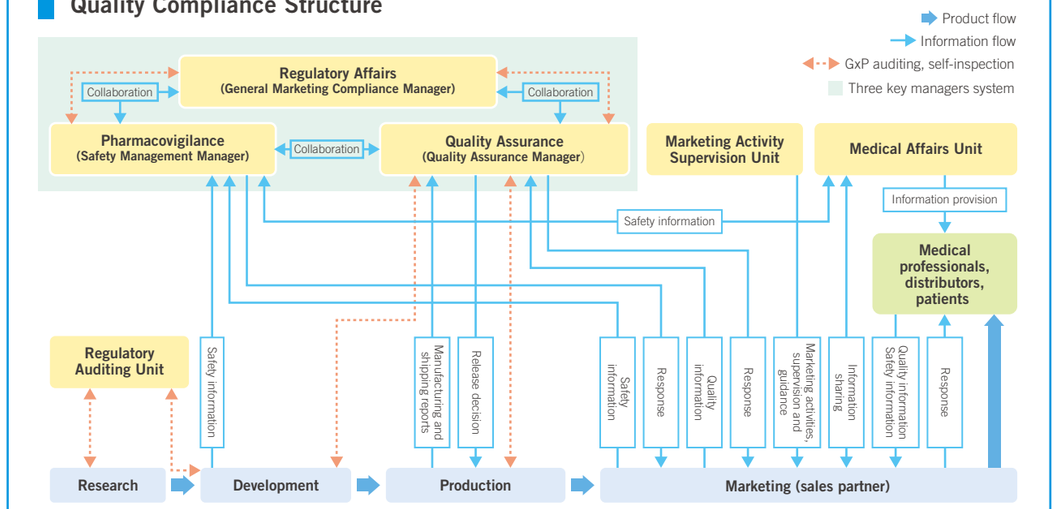
ISO 13485 is an international standard for quality management systems established by the International Organization for Standardization (ISO) that prescribes requirements concerning the design, development, and manufacturing of medical devices. In Japan, ISO 13485 has been adopted as an ordinance on standards for manufacturing control and quality control of medical devices and in vitro diagnostics.

Laws and Regulations Governing Pharmaceuticals and Medical Devices

Life cycle	1 Basic research	2 Development	3 NDA	4 Manufacturing, quality control, information provision, and product provision	5 Post-marketing
Laws and Regulations: Pharmaceuticals	• PMD Act • GLP	• PMD Act • GLP • GCP • GMP for investigational products	• PMD Act	• PMD Act • GMP • GQP	• PMD Act • GPSP • GVP
Laws and Regulations: Medical devices	• PMD Act • GLP	• PMD Act • GLP • GCP • QMS	• PMD Act	• PMD Act • QMS	• PMD Act • GPSP • GVP

- PMD (Pharmaceutical and Medical Device) Act
  Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices
- GLP: Good Laboratory Practice
  Standards for conducting non-clinical studies on safety
- GCP: Good Clinical Practice
  Standards for conducting clinical studies
- GMP: Good Manufacturing Practice
  Standards for manufacturing control and quality control in manufacturing
- GVP: Good Vigilance Practice
  Standards for post-marketing safety management of drugs, quasi-drugs, cosmetics and medical devices and regenerative medicine products
- GQP: Good Quality Practice
  Standards for quality control of products
- GPSP: Good Post-marketing Study Practice
  Standards for conducting post-marketing surveys and studies on drugs
- QMS: Quality Management System
  Ordinance on Standards for Manufacturing Control and Quality Control of Medical Devices and In Vitro Diagnostic Reagents

Quality Compliance Structure



Safety management

Sometimes side effects not observed in the development stage come to light after the launch of a new pharmaceutical product. In accordance with Good Vigilance Practice (GVP) standards, Seikagaku conducts post-marketing pharmacovigilance activities involving promptly and appropriately collecting, evaluating, and sharing feedback information on the side effects of pharmaceuticals prescribed at medical facilities. Through these activities, we prevent the expansion of side effects and promote safety assurance and appropriate use of new drugs.

Medical information collection and provision activities

Seikagaku has established the Medical Affairs Unit, which engages in activities to provide current scientific knowledge to external professionals independently from the marketing division. As scientific experts with sufficient ethical perspective, the unit contributes to medical progress by creating and disseminating medical evidence relating to disease information and products in the fields in which Seikagaku focuses, such as orthopedic disorders and ophthalmic diseases.

Topics

Measures to strengthen data integrity by cooperating with quality assurance departments

To provide a stable supply of high-quality pharmaceuticals and medical devices, the Quality Assurance Department engages in activities to develop and maintain a quality management system based on our Quality Policy.

These days, ensuring data integrity is important not only in operation of the quality management system for existing products, but also in the pursuit of new drug development and overseas business development. The department supports quality operations company-wide through operation of a quality operations management system as well as use of a document management system for handling documents and records in accordance with GxP standards.

To strengthen data integrity, the Quality Assurance Department cooperates with quality assurance departments, including those at the plants and laboratories, in utilizing systems and executing quality operations to ensure continuous quality assurance.

A Quality Assurance Department staff meeting to support quality operations

HUMAN RESOURCES

Seikagaku aims to develop self-driven and self-disciplined employees who can create new value and contribute to sustainable corporate growth.

Development of human resources

Seikagaku Corporation considers human resources to be an important corporate asset and seeks people who understand and put into practice our core values “creativity,” “fairness,” and "dreams and passion” and are capable of self-growth while fulfilling their roles with a sense of responsibility.

Seikagaku also strives to provide fields for each person to grow and thrive in. We endeavor to cultivate autonomous employees who go about their work with enthusiasm and pride and produce results. We promote upskilling and career development through a combination of systematic education in various training programs, workplace education through day-to-day work, and job rotation.

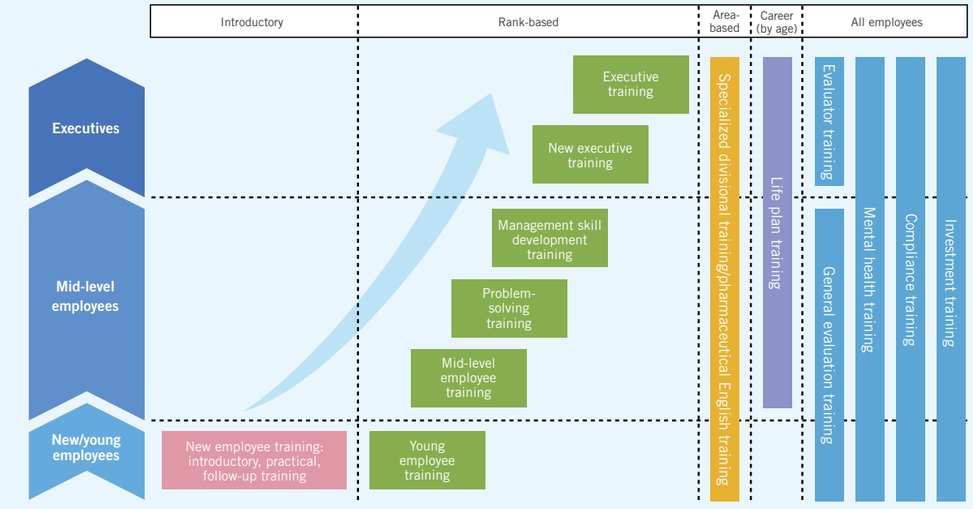
The curriculum for systematic education is depicted in the diagram below. We conduct a variety of training programs for everyone from young employees to executives with the objective of promoting the growth of individual employees and the Company. In response to the spread of COVID-19, we continue to switch from group training to online training.

Work-life balance

To help its employees achieve a good work-life balance, Seikagaku has introduced flextime at all business sites, including laboratories and plants, and established a weekly “no overtime day.” To help employees balance their personal lives with their work, Seikagaku encourages them to develop their own work styles. For example, we now have a reduced-working-hours system for employees who provide childcare and nursing care, and employees may also accumulate lapsed annual paid leave for use during prolonged illnesses or to cope with extended childcare and nursing care needs. In the fiscal year ended March 31, 2021 (fiscal 2020), we instituted a work-from-home system as an option for diversifying work styles. Other objectives for introducing this system were to increase productivity though greater operational efficiency and create a means of maintaining continuity of operations in the event of a disaster.

Employees used an average of 70.2% of paid leave in fiscal 2020. From fiscal 2007 to fiscal 2020, 100% of staff who left work for childcare reasons returned, and the number of male employees taking childcare leave has also increased. Furthermore, Seikagaku creates employee-friendly workplaces through staff assignments that correspond to the nature and amount of work, improvement of workplace environments, and by limiting long working hours.

Training Systems



Diversity management

Seikagaku is creating an environment and developing systems, programs, and mechanisms to enable female employees to fully demonstrate their capabilities and is implementing measures to support the advancement of women as part of diversity management efforts.

In 2016, we launched a project to promote women’s advancement in the workplace and raise awareness within the company. Since then, we have engaged in activities to improve internal systems based on comments made in interviews with all female employees. As of March 31, 2021, the ratio of female managers was 16.9%, a sharp increase from 7.9% four years earlier.

In fiscal 2019, we changed the project into a diversity and inclusion project. To ensure that the contributions and successes of diverse employees are the driver of Seikagaku’s sustained growth, we have set concrete targets for each business site and are proceeding with reforms to create an organization in which individuals can demonstrate their full potential.

Mental healthcare

Since 2009, Seikagaku has implemented measures aimed at maintaining the physical and mental health of employees to vitalize workplaces and increase productivity. Specifically, we are improving the overall workplace environment by obtaining the advice and assistance of industrial physicians and public health nurses periodically and as needed, by conducting mental health care seminars for managers that utilize the results of annual stress checks, and other means. We have also instituted an external hotline and counseling service that employees and family members can freely utilize and are developing a self-care support system to enable employees themselves to recognize physical disorders and stress and learn how to cope with them.

COVID-19 infections countermeasures

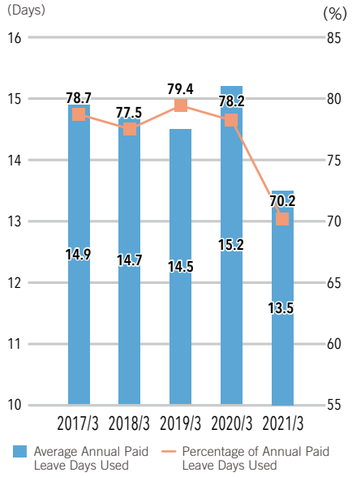
Seikagaku is implementing infection prevention measures that give the highest priority to our business partners, employees and their families, and local residents. We prudently review this arrangement in accordance with the current infection situation and other considerations and strive to raise employee awareness by circulating information internally about key points and rules concerning infection prevention.

As a rule, in workplaces where working from home is a practical solution, we instruct employees to do so. We are changing commuting methods and expanding operation of a flextime system to prevent COVID-19 infections while also realizing flexible work styles for employees.

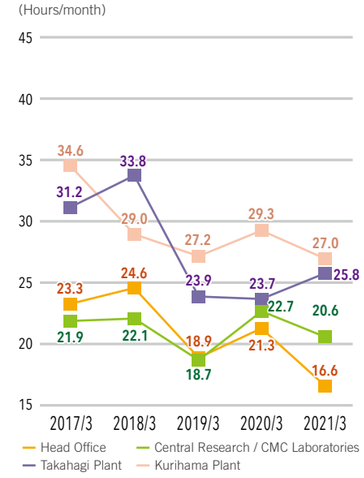
From July to September 2021, we strove to prevent the spread of infection by providing workplace COVID-19 vaccinations for about 600 employees and their family members and employees of business partners who wished to be vaccinated.

*Information in this section is current as of September 30, 2021.

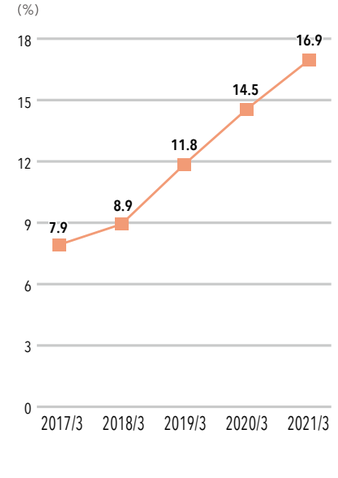
Use of Paid Leave



Average Overtime Hours by Business Site



Executive Positions Held by Women



*The figures provided on this page are all on a non-consolidated basis.