

Resolving Healthcare Challenges

Enriching LIFE with Healthcare Solutions

In the midst of a drastically changing healthcare environment, Terumo is working to solve healthcare challenges from a long-term perspective by focusing on the following three sustainability priorities. These are aimed at ensuring all people can receive optimal healthcare with peace of mind, allowing them to live fulfilling lives in line with their individual lifestyles.

- Providing healthcare that is closely aligned with the life of each individual
- Co-creating a sustainable healthcare system
- Spreading medical technologies and services and improving access to healthcare

Aiming to Make a Positive Contribution to Diabetes Treatment Providing Products and Solutions to Support Each Individual Patient

Diabetes is well-known for leading to complications (such as retinopathy, neurological disorders, renal disease, myocardial infarction, strokes, etc.), and treatment of diabetes must be tailored to the pathology of the individual patient. As of 2019, worldwide, around 463 million people*1 were suffering from diabetes. In Japan, according to survey results compiled by the Ministry of Health, Labour and Welfare (MHLW), since 1997 there has been a steady increase in the number of people who are strongly suspected of having diabetes, and the total is estimated to have reached around 10 million people*2 in 2016.

When treating diabetes, it is important to prevent the disease from progressing, and to prevent the development of complications. For this reason, patients need to control their blood glucose levels carefully on a daily basis. Besides the challenges posed by daily care, patients are also affected by the constraints on their day-to-day activities and by society's attitudes towards them, and as a result they often experience not only physical problems but also mental and emotional stress.

For approximately 40 years, Terumo has provided the products needed for the diagnosis and treatment of diabetes, including the insulin syringe with staked needle, which was introduced in 1982, the blood glucose monitoring system, in 1993, and the world's thinnest pen needle for insulin use, in 2005. We aim to develop and provide products and systems that reflect an understanding of diabetes patients' daily lives and feelings, and which provide value for both patients and healthcare professionals.

The world's thinnest pen needle for insulin use, launched in 2005, was developed with the aim of reducing the physical and mental burden of daily injections on patients, and contributing to improving their quality of life. To reduce the pain of the needle puncture, the tip was designed with an asymmetrical blade surface structure so that it makes a small cut with a razor-sharp edge rather than having the needle pierce the skin.

In 2018 we launched sales of Japan's first insulin patch pump. Insulin pumps are used to administer insulin to those with Type 1 diabetes or to people with Type 2 diabetes whose insulin secretion has significantly dropped. Terumo has eliminated the tubing that connects the insulin infusion unit to the pump and integrated the pump function into the infusion unit to create a patch-type structure that can be operated with a remote control so that patients carry out their daily lives normally, including work and housework. In addition to this diverse product portfolio, we are focusing on developing IT systems and digital solutions utilizing AI and other digital technology to support treatment aligned with the status of each individual patient.

In 2020, Terumo and MICIN, Inc. began joint development in Japan of a diabetes digital treatment support system. The goal is to support the treatment of diabetes based on information about individual patients' blood glucose levels, diet, exercise, and medications.

Overseas, in 2020 we began joint development of an automated insulin delivery system with Diabeloop of France. Linked to glucose concentrations in subcutaneous interstitial fluid measured with a continuous glucose monitoring device, the system automatically administers the right dose of insulin from an insulin pump according to the patient's condition. In 2021, we also partnered with Glooko, a U.S.-based company, with the goal of advancing the digitalization of diabetes treatment. Glooko is developing



Needle for pen injector used for self-injection



Detachable insulin patch pump



Patient wearing the detachable insulin patch pump

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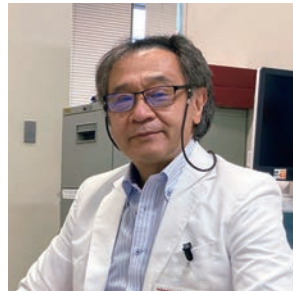
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diabetes data solutions that allow centralized management of data related to diabetes treatment, including blood glucose levels and insulin dosage, and currently provides solutions in 27 countries. By managing and visualizing data from Terumo's insulin patch pumps and blood glucose meters on the system, we aim to utilize the data to allow patients who use these devices to manage their disease themselves, as well as in examinations and guidance by medical professionals.

The year 2021 marks the 100th anniversary of the discovery of insulin, and also the 100th anniversary of the founding of Terumo. Going forward, Terumo will continue to provide support to help build a better future for diabetes patients, by paying attention to the daily lives and feelings of diabetes sufferers, and by providing products, systems and solutions that create value for both patients and healthcare professionals.

*1 International Diabetes Federation (IDF), *IDF Diabetes Atlas* 9th edition, 2019, Estimated number of adults with diabetes <https://diabetesatlas.org/en/>

*2 Ministry of Health, Labour and Welfare (MHLW), 2016 National Health and Nutrition Survey (Japanese only) <https://www.mhlw.go.jp/stf/houdou/0000177189.html>



Tomoyuki Kawamura, M.D., Ph.D.
Department of Pediatrics, Osaka City University Graduate School of Medicine

Voice

I have been treating patients with Type 1 diabetes for more than 30 years. Type 1 diabetes absolutely requires blood glucose monitoring several times a day and insulin injections along with diet and exercise. The patient needs to self-manage their blood glucose level daily to ensure it stays within the target range. Failure to do so increases the risk of future complications. Type 1 diabetes occurs regardless of lifestyle habits or constitution. The sudden onset of the disease in a healthy person places a heavy psychological burden on the patient, and blood glucose monitoring and insulin injections can be painful and difficult.

Products related to the treatment of Type 1 diabetes include Terumo's blood glucose meters and insulin needles, as well as an insulin patch pump, which I assisted in developing. What I sense in using these Terumo products is a closeness between the engineers and developers, and between the patients and us—and I think this is one of the strengths of being a domestic manufacturer. With some of these products, we have had the opportunity to sit down with patients and listen to their opinions, and the experience of seeing improvements made that quickly incorporated that feedback. I look forward to seeing Terumo continue to demonstrate these strengths in many directions.

Delivering Efficiency and Quality to Cell Therapy Manufacturing

Applying Automation to the Challenges of Manual Cell Therapy Manufacturing

Cell therapy, which is the practice of processing and culturing harvested cells and using them to treat disease, and gene therapy, which is the treatment of disease by administering gene-modifying agents or gene-modified cells into the human body, are resulting in new treatment methods. Research and development is actively ongoing in various disease areas, and practical application of these methods is steadily progressing. For example, CAR-T cell therapy, which was approved as a new treatment for leukemia, is an autoimmune therapy in which a protein receptor called a chimeric antigen receptor (CAR) is introduced into T cells taken from the patient's own blood. These cells are multiplied in the lab, then reinfused to the patient, and the CAR T cells fight the cancer cells. As another example, mesenchymal stem cells from the bone marrow of a healthy donor can be cultured and transplanted into a patient.

Manufacturing cell and gene therapy products requires an enormous amount of work, including the collection and cultivation (expansion) of cells, formulation and filling of final cell therapy products in bags, and data recording and other documentation. Currently, many of these tasks are done manually, and in addition to the time required, there are issues such as the cost of clean rooms and other facilities, labor costs, risk of contamination during the process and risk of bacterial contamination.

Contributing to the Field of Cell Therapy R&D and Manufacturing by Automating the Process

Terumo Blood and Cell Technologies, one of the Terumo Group's three companies, has been automating the collection and processing of blood and cells for decades. Utilizing the technology cultivated through years of experience, the company aims to contribute to the research, development and manufacturing of cell and gene therapy products, which require a lot of manual work, by providing products that improve the efficiency of workflow from cell collection to the treatment of patients.

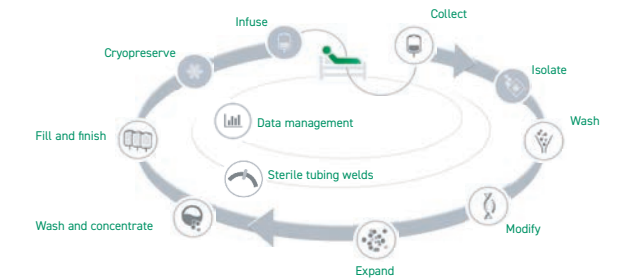
The company's centrifugal apheresis system is used in therapeutic apheresis: The blood of a donor or patient is circulated outside the body, certain blood components are extracted or removed by centrifugation, and the other components are returned to the body. Recently, the system has also been used to collect cells that are the raw material for various cell therapies, such as CAR-T cell therapy.

In the cell expansion process, it is important to increase the number of cells efficiently while maintaining quality. Terumo Blood and Cell Technologies' cell expansion system is equipped with sterile disposable cell expansion sets in a closed system where the cells do not come in contact with the outside air. By automating tasks such as performing media exchanges to feed cells and remove wastes, which are time-consuming and error-prone when done manually, we aim to achieve more efficient and stable cell expansion compared to conventional manual expansion while maintaining cell quality.

While the processes of cell collection and expansion are becoming increasingly automated, the filling and finishing processes are often done manually, which may affect the viability and functionality of the cells. The fill and finish system of Terumo Blood and Cell Technologies automates the filling process and allows the user to change the settings according to the type of cell therapy product and the required volume. The electronic recording of the work process also facilitates compliance with current good manufacturing practices (cGMP).

By providing such products as a system, Terumo Blood and Cell Technologies will contribute to the development and spread of cell and gene therapy, increasing treatment options for patients.

The Cell and Gene Therapy Production Cycle
(Process details vary depending on therapy application)



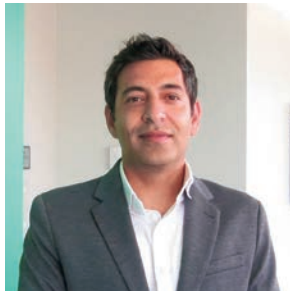
Cell expansion system



Cell therapy fill and finish system

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Dalip Sethi, Ph.D.
Scientific Affairs Director,
Terumo Blood and Cell Technologies

Voice

The production and delivery of cell-based therapies is a complex and logistically challenging process. Cell production and formulation processes are often developed in research laboratories and typically include many labor-intensive tasks with the risk of error. Therefore, there is a huge demand to automate those manual processes. This is where our automated cell expansion system and fill and finish system make an enormous contribution in taking those processes from manual to automated. These systems are also expected to lower the risk of contamination as they are functionally closed systems which reduce open events. With our technologies, we help cell therapy developers and researchers simplify processes while increasing accuracy, consistency, reliability and reproducibility to deliver the therapies that patients need.

Aiming to Generate Innovation that Contributes toward the Future of Healthcare Terumo Bay Area Innovation Lab

A Group of Experts with Diverse Nationalities and Backgrounds

Terumo locates its R&D bases in the regions most appropriate for the products that they are working on, in order to respond to next-generation healthcare needs as speedily as possible. In 2018, we founded the Terumo Bay Area Innovation Lab (TBAIL), a new R&D base located in California's Silicon Valley which has brought together technologies and engineers from all over the world.

The TBAIL R&D base was formed through the integration of Kalila Medical, Inc. (KMI), a U.S. company that became part of the Terumo Group in January 2017, and Terumo's Silicon Valley Lab (SVL), the associates of which included personnel on assignment from Terumo's Corporate R&D Center in Japan; both of these organizations had facilities located in the Bay Area. TBAIL has approximately 50 associates whose work is primarily centered in product development for the Cardiac and Vascular Company (one of Terumo's three companies), research and development, pilot production, and bridge production (small-scale production conducted prior to ramping up to large-scale).

The associates who work at TBAIL come from diverse nationalities and backgrounds, many of them have specialized in medical devices in their careers, and each of them is an expert with specialized knowledge and skills. Like a start-up company, we bring our technologies and know-how to each other in order to commercialize our products and promote projects speedily through cooperation.



Terumo Bay Area Innovation Lab (TBAIL)



Associates Working at TBAIL

Leveraging Silicon Valley's Geographical Advantages to Contribute to the Future of Healthcare

In Silicon Valley, there are many start-ups with new technologies in the medical device field, companies that own production facilities and are responsible for production, and consulting companies that specialize in collaborations with U.S. medical facilities and regulatory applications, forming an industrial cluster.

In order to take advantage of this environment to search for new technologies and ideas and to promote the initial development of products, Terumo invested in a Silicon Valley venture fund in 2013, and in 2014 established Terumo Medical Innovation Inc. (TMI), a development subsidiary located in a hospital. In 2018, TBAIL was established based on the concept of "Terumo's R&D campus that anyone can use," and the development projects that were initially developed at TMI were transferred to TBAIL. TBAIL will also be expected to promote research and development by the entire Terumo Group in a rapid, more innovative manner through joint development with start-ups and academia.

To date, TBAIL has mainly been developing devices used in interventional therapy for cardiovascular and peripheral diseases. Among them, a steerable sheath used in the treatment of arrhythmia called catheter ablation has been launched in the U.S., Japan and other countries and is being used in medical settings. Going forward, TBAIL will continue to actively engage in technological collaboration within the Terumo Group and themes outside of the Cardiac & Vascular Company, while also strengthening our search for and development of technologies in fields essential to future healthcare, such as biotechnology and digital health, with the aim of creating new innovations that will contribute to future healthcare.



Yuichi Tada
Principal R&D Engineer,
Silicon Valley Lab

Voice

We moved our base of operations from Japan to the U.S. in order to launch our newly developed products based on the needs of the medical field in the U.S., the largest market in the world. We often face difficult technical challenges, but we overcome them with positive thinking and smiles together with local associates who have different expertise and cultural backgrounds. We are also searching for new technologies to realize the future of medicine, and developing products through partnerships with start-ups. We will continue to contribute to the creation of healthcare that the era to come will need by demonstrating the true spirit of corporate R&D, which is based on taking on challenges and trial and error.



Irene Tan
TBAIL Director/Site Leader

With TBAIL being a small environment, my responsibilities include hands-on involvement with production of our commercially released device and Design control activities for four R&D projects. I have observed that having a small group onsite advantageously allows team members from each project to share equipment, ideas and past experiences that can benefit current projects. Associates are cooperative with each other and communicate well. Within each project, I openly share my experiences, suggest improvements, and ensure that quality procedures are being followed. I hope to guide the project teams in an efficient manner and contribute to the design, testing, manufacturing, and release of future Terumo products.