Enzyme Wave

2013

Volume 16

The Shrine Management Agency ©神社司庁

AMANO

Enzyme Wave vol.16

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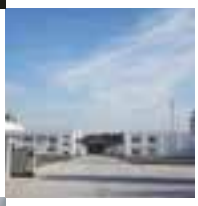


Mifunashiro Hounou-shiki

One of the ceremonies in the *Shikinen Sengu*, this process involves dedicating the case used to carry the sacred effigies from the old to the new shrine building.

Members of the Shrine Management Agency ©神社司庁

Ise Shrine, the Land of Eternal Youth

This October, Ise Shrine will undergo a ritual performed every two decades called *Shikinen Sengu.* Although *Shikinen Sengu* is a celebrated event in Japan, not many people are aware of its significance.

Shikinen mean "the designated year of the ritual" which in the case of Ise Shrine is every two decades. The term *Sengu* (also called *Senza*) refers to the reconstruction of the shrine building and the relocation of the sacred effigies. Shrines all across Japan hold *Senza* festivals where they repair and renovate their facilities from time to time. However, Ise Shrine is unique in the sense that the *Shikinen Sengu* festival requires the reconstruction of an exact replica of the shrine building as the new home for the effigies. This tradition has been observed for over 1,300 years.

The reconstruction project is currently under way at a holy site adjacent to the old shrine building. The sites, one in the east and one in the west, will continue to be used alternately every twenty years.

The shrine building was initially built in the style of a granary for storing crops. This design has stayed the same through each rebuilding throughout 1,300 years. In our daily lives, we come across many old things that retain their old form as well as many new things that possess new shapes. Nevertheless, it is rare that we see something new that has been completely remade in its old form. The *Shikinen Sengu* ritual ensures this reincarnation will continue in the same manner for ages to come.

Ise Shrine has experienced its share of trials and tribulations during its 13-century history of *Shikinen Sengu*. During the latter half of the Muromachi Era around the 15th and 16th century, the shrine was unable to perform *Shikinen Sengu* for more than 100 years. Instead of holding the official ritual, the shrine built a makeshift structure to house the sacred effigies while the old building underwent renovations. A warlord from the Aichi region named Oda Nobunaga eventually came to the rescue and provided the shrine with funds equivalent to 300 million yen in today's currency. Although Nobunaga was unfortunately defeated in a *coup d'etat* called the Honno-ji Incident in 1582, his successor, the warlord Toyotomi Hideyoshi, carried on Nobunaga's will and helped organize the 41st *Shikinen Sengu* in 1585 during which the *Naiku* (Inner Shrine) and *Geku* (Outer Shrine) were reconstructed. After Tokugawa Ieyasu unified Japan, it was decided that the Tokugawa Shogunate would finance the Ise Shrine so it could resume holding *Shikinen Sengu* on a regular basis. A period of stability finally arrived and commoners were able to make pilgrimages to this holy place. Nobunaga, Hideyoshi and Ieyasu, the three great warriors of Aichi, had consequently helped Ise Shrine prevail over a time of hardship and suffering.

Supported by many figures in both past and present, the old and yet new sacred grounds of Ise Shrine continue to preserve its eternal youth into the Heisei Era of today.

Main building of the Inner Shrine (courtesy of the author)

About our guest columnist

Kiyomi Chikusa／Author and adjunct instructor at Kogakkan University

Ms. Chikusa was born in Tsu City, Mie Prefecture. After graduating from Tsu Prefectural High School and then Jissen Women's University in Tokyo, she returned to her hometown and became a production assistant at the Tsu Branch of the NHK national television station. Following a stint as chief editor of the local magazine *Ise Shima*, she decided to become a full-time writer based in Mie Prefecture. In 2006, she started writing a regular series titled Ise, the Eternal Holy Land for the Shinkansen newsletter *Gekkan Hitotoki* and to this day has contributed 80 installments. At Kogakkan University, she teaches a regional science course called Ise-gaku as well as a course called Exercises in Expression which aims teach students methods to improve their writing and self-assertion skills. Her works include *Oise, Toriimae Okage Engi* published by Kodansha and *Eien no Seichi, Ise Jingu* and *Ise Jingu, Tokowaka no Seichi* published by Wedge. Ms. Chikusa wrote the scripts for all ten installments of a television series called Oise-san broadcast by Mie Television Broadcasting Co., Ltd. She is a member of the Japan Society for Studies in Journalism and Mass Communication.

Technical Report

Participation in the NITE Program to Access International Genetic Resources

The Convention on Biological Diversity and the Access and Benefit-Sharing Issue

Signed in 1992 and entering into force in 1993, the Convention on Biological Diversity (CBD) has three fundamental goals that are:

1. conservation of biological diversity (or biodiversity);
2. sustainable use of its components; and
3. fair and equitable sharing of benefits arising from genetic resources

Agreement concerning the third goal of access and benefit-sharing (ABS) has remained elusive because of conflicts of interest between the providers (primarily developing countries) and users (primarily developed countries) of genetic resources. However, this conflict was finally resolved during the 10th meeting of the Conference of the Parties (COP10) held in Nagoya, Japan, in October 2010 when the convention implemented a legally binding international regime to ensure proper ABS in the resulting Nagoya Protocol.

The CBD and the Nagoya Protocol now require users to gain permission from providers and also for both contracting parties to reach an understanding in terms of ABS. Nevertheless, many problems still persist in regards to relations between countries and corporations. For example, it is still difficult for a private corporation to negotiate benefit-sharing with a provider government and access genetic resources in compliance with domestic laws and regulations.

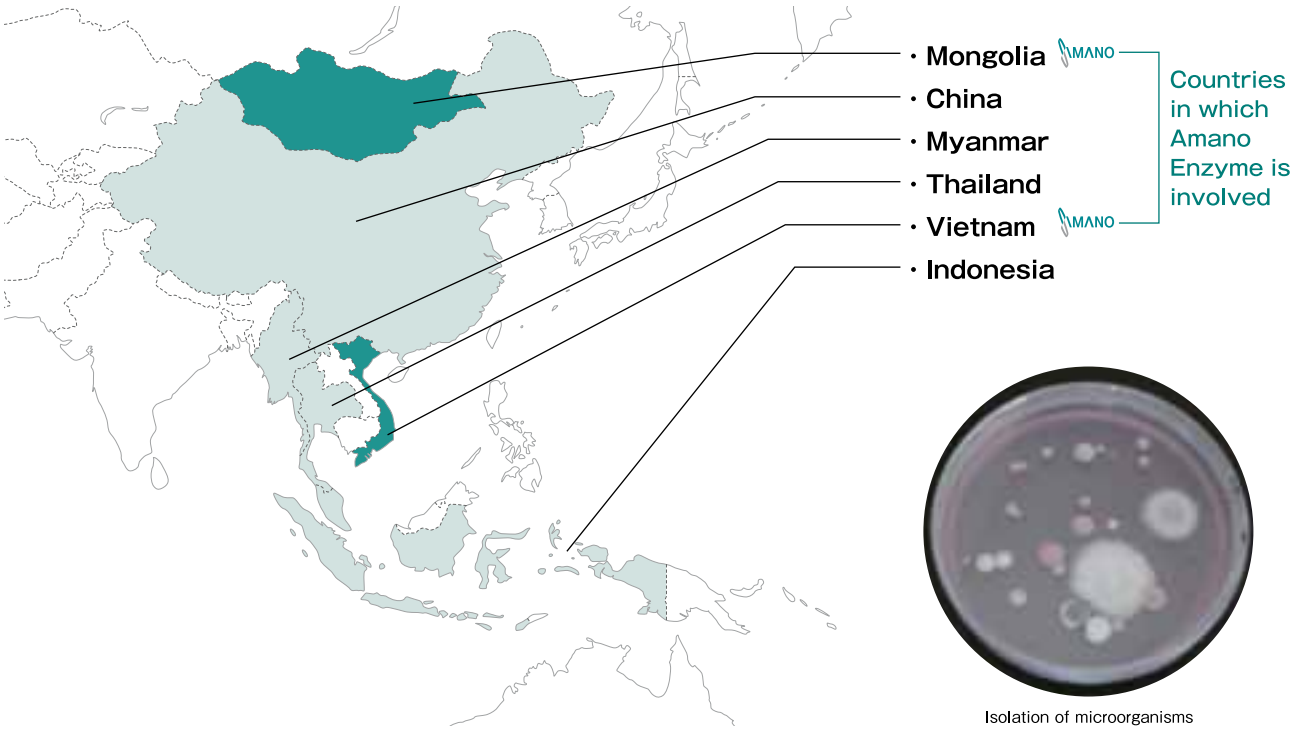
The NITE framework for ABS

The National Institute of Technology and Evaluation (NITE), a government-affiliated agency in Japan, has been working on this issue from early on. NITE began building a framework for accessing genetic resources from microbial genetic material during a joint project with an Indonesian research institute to screen microorganisms that started in 2003. With the help of Indonesian researchers, NITE was able to send isolated microbial species to its biotechnology headquarters in Japan for preservation.

NITE has become also collaborated with organizations in Myanmar, Vietnam, Mongolia and other Asian countries in similar microorganism screening projects. The agency has now established a framework where it solicits the participation of private corporations that are allowed to travel to various regions to isolate biological material for their own specific purposes.

NITE's framework demonstrates one way of

NITE microorganism screening operations in various countries



resolving the ABS issue. Users can access genetic resources, and providers can not only collect microbial utilization fees and royalties from commercialization, but also acquire valuable microbial screening technology.

Such joint projects are beneficial for corporations not only from the perspective of product development. They also let firms contribute to preservation and sustainable use of microbial resources, one of the major aims of the CBD. Furthermore, these projects can lead to a higher level of international cooperation in the Asian Pacific region.

The screening of new enzyme at Amano Enzyme Inc.

Amano Enzyme Inc. became one of the members of NITE's joint project in 2012. In July and August of that year, we began performing microbial isolation operations in Mongolia with the cooperation of the Institute of Biology at the Mongolian Academy of Sciences. We also initiated a similar program in Vietnam in November and December in partnership with the Institute of Microbiology and Biotechnology at the Vietnam National University. In these efforts, we screen various types of local soil or fermented foods for microorganisms, which we then culture in a species-specific manner. In a short period of time, we have been able to isolate 450 Mongolian and 632 Vietnamese microbial species, including filamentous fungi, actinobacteria and bacteria, and ship them to Japan. In Mongolia, we screened for microorganisms in fermented dairy products as well as different types of soil categorized according to climate and vegetable growth properties. In Vietnam, we screened for microorganisms in fermented fish products and in soil from forests in the northern regions and subequatorial jungles in the south. We hope this work will lead to the isolation of novel microbial species from environments and foods inaccessible in Japan.

Amano Enzyme Inc., we use a proprietary microbial library to screen for enzymes with the potential to benefit people's lives. We are also trying to discover new kinds of enzymes from microorganisms in Mongolia, Vietnam and other faraway places that cannot be obtained from microbial genetic material indigenous to Japan.

In order to ensure proper benefit-sharing, we compensate research institutes in provider countries with fees for microbial resource utilization and a part of our profits from commercialization. In this manner, our international operations aspire to contribute to the preservation of biological diversity and the sustainable use of natural resources.

Sükhbaatar Square in Mongolia

The Ho Chi Minh Mausoleum in Vietnam

A plateau in Midwest Mongolia

A tropical forest in Vietnam

The Asahi Shimbun ©朝日新聞社

Topics 1 A New Regulatory Framework for Enzymes in Europe: — FIAP(Food Improvement Agents Package) Regulation(EC)Nos.1331/2008

As part of the Food Improvement Agents Package (FIAP), the European Union established a set of rules on food enzymes known as Regulations (EC) No. 1332/2008, which came into effect on January 20, 2009. The following amendments have been made since:

July 2009	The European Food Safety Authority issued guidelines on safety assessment
March 2011	The EU issued submission protocols
June 2012	Regulation (EU) No. 562/2012 allows the submission of a Grouped application dossier for enzymes obtained from: edible parts of plants or animals with such enzymes possessing the same catalytic activity and processed from the same source material with a substantially same production process; microorganisms having the status of Qualified Presumption of Safety; and microorganisms authorized in either France or Denmark in accordance with the SCF guidelines of 1992

The main points of the FIAP are as follows:

■Expansion of regulatory coverage

- The FIAP covers all food enzymes including processing aids that were previously exempt under Directive No. 89/107/EEC for food additives. However, it does not cover food enzymes used to produce food additives and processing aids, and food enzymes intended for human consumption for nutritional or digestive purposes.
- The FIAP covers enzymes used to produce food to be exported to Europe.

■Implementation of a pre-market authorization system based on safety assessments

- Enzymes that have not undergone common authorization procedures according to Regulation No. 1331/2008 or food produced with such enzymes cannot be marketed in the EU.
- Food enzymes covered under Regulation No. 1829/2003 regarding genetically-modified foods and animal feed must undergo authorization under this reguation in addition to authorization under FIAP regulation.

■Creation of a Community List of Approved Enzymes

Enzymes that have undergone safety assessment by the European Food Safety Authority (EFSA) and have been authorized by the European Commission will be added to a Community List of Approved Enzymes that is currently under development. This list includes the following entries:

> The International Union of Biochemistry and Molecular Biology (IUBMB) nomenclature; specifications, including IUBMB no., origin, purity criteria (JECFA specs), etc.; the foods to which the enzyme may be added; the conditions under which the enzyme may be used; restrictions on enzyme sale; and specific labeling requirements

■Labeling requirements

Enzymes or enzyme preparations must fulfill the following labelling requirements which came in force on January 20,2010. However, food enzymes or their preparations that were sold or labeled before January 20, 2010, can still continue to be distributed provided they have not reached their expiration date.

> The name of the food enzyme; the statement “for food” or the statement “restricted use in food” or a more specific reference to its intended food use; preservation conditions; usage conditions; batch/lot numbers; precautions for use; the names and addresses of all manufacturers, packagers and sellers; the maximum amount of ingredients or ingredient groups allowed in food under quantitative restrictions; net quantity; enzymatic activity data; expiration date; allergy data; all ingredients (in order of % of mass)

■Interim measures

【Procedures for existing enzymes】

- Enzymes such as lysozymes, invertases, ureases (for wine) and β-glucanases (for wine) that were regulated by other laws have been approved for addition to the Community List.
- Other existing food enzymes will undergo the following procedures for authorization.

An authorization application should be submitted to the European Commission by March 11, 2015
↓
The European Commission will forward the application to the EFSA and receive opinions regarding safety
↓
Based on the opinions from the EFSA, the European Commission will prepare an entry in the Community List of Approved Enzymes, which is scheduled to be released around 2020.
↓
National provisions in force concerning the placing on the market and use of food enzymes and food produced with food enzymes will continue to be applied in the Member States (e.g. France, Denmark) until the Community List is established.

【Procedures for new enzymes (i.e., those to apply for authorization after March 11, 2015)】

<Before establishment of the Community List> As with existing enzymes, dossiers for new enzymes need to be submitted to the European Commission for authorisation. They will however not be listed in the first Community List. As the list is upgraded periodically, such enzymes can be regulated and sold in individual countries until the list is published. If the product is to be sold in France or Denmark, it will need to be submitted for approval under the laws of those countries.

<After establishment of the Community List> As with the existing enzymes, dossiers for new enzymes need to be submitted to the European Commission for authorisation. Until the enzymes are listed in the Community List, they cannot be sold in the EU. According to the European Commission, the process for safety assessment and approval is expected to take approximately 21 months.

■Food additives approved for use in enzyme formulations

Annex III of Regulation No. 1333/2008 lists the food additives and their maximum quantities that can be used in enzyme formulations.

After December 2, 2013, food additives not included in this list cannot be used for enzyme formulations to be sold in Europe.

Amano Newsletter

Amano News Letter

New plant opening at Amano Enzyme Manufacturing (China) Ltd. (AEMC)

AEMC completed construction of a new plant in June 2012. The plant, which began full-scale operations in August of the same year, stands on a site of about 40,000 m^2 and has a total floor area of about 10,000 m^2, approximately twice the size of the old facility. It is anticipated to help AEMC significantly expand its capacity to manufacture final products. As a production base for enzymes for the Asian region, AEMC is committed to satisfying our customers through its quality product.

View from the entrance of the new plant

Opening of the Amano Enzyme Asia Pacific Office (AEA)

AEA opened its doors in Kuala Lumpur, Malaysia, in June 2012.

The emerging nations of Asia as well as countries in Oceania are undergoing rapid economic growth and are expected to become incredibly large markets in the near future. Moreover, these markets are anticipated to be important for Amano Enzyme. We hope AEA will act as a base for market surveys of this region and enable us to of this region while valuing long-lasting relations with our customers.

Inside the AEA

Topics 2

Circumstances Surrounding the Observance of *Halal* Rules by Japanese Companies

The 1.8 billion Muslims in the world today represent about 25% of the global population, and it is estimated that their number will rise to 3 billion by 2025. Although only 100,000 Muslims live in Japan (among which 10,000 are citizens), mosques have been providing religious services in the country for many years. The first mosque in Japan was built in 1931 in Nagoya, Aichi Prefecture. Other mosques were eventually established, the more well-known and historical ones being the Kobe Muslim Mosque in the Chuo Ward of Kobe, Hyogo Prefecture, and the Tokyo Camii in the Shibuya Ward of Tokyo for Turkish observers. There are now more than 70 mosques and houses of worship for Muslim residents and converts in Japan.

The term *halal* designates objects and actions that are lawful under the Sharia laws of Islam. The opposite of *halal* is *haram*, which designates what is prohibited. *Syubhah* is a term for anything that does not readily fall under *halal* or *haram* definitions.

All things created by Allah are considered to be halal, except for those that are explicitly forbidden. Items that are *haram* include anything derived from pigs such as meat, lard, pigskin byproducts (e.g., gelatins and collagens), organs, bones (e.g., to make activated charcoal) and fur; dogs; blood and blood byproducts; improperly slaughtered animals; and *khamar*, the term the Quran uses to indicate intoxicants such as alcoholic beverages. Use of such items is prohibited mainly because they are believed to be unclean and therefore harmful.

To be precise, at the heart of this Muslim rule concerning what is lawful and forbidden lies two major concepts: one is the *halal* rule as just described and the other is *halalan thoyyiban*, which means wholesome. *Halalan thoyyiban* encompasses the ideas of healthiness, safety, nourishment and quality. The *halal* rule covers not only food but also a whole range of food-related elements from additives to supplements to eateries. In recent years, the definition of *halal* has been expanded greatly to incorporate cosmetics, pharmaceuticals, toiletries, leather goods and even financial activities such as bank and insurance services.

The *halal* industry is estimated to have a market scale of about US$ 2.1 trillion, of which food accounts for about US$580 billion. Multinational corporations, especially those operating in Southeast Asia, are becoming increasingly aware of the importance of gaining *halal* certification. Muslims are obliged to consume only those foods that meet *halal* standards, meaning they will preferentially purchase *halal* over *haram* imports.

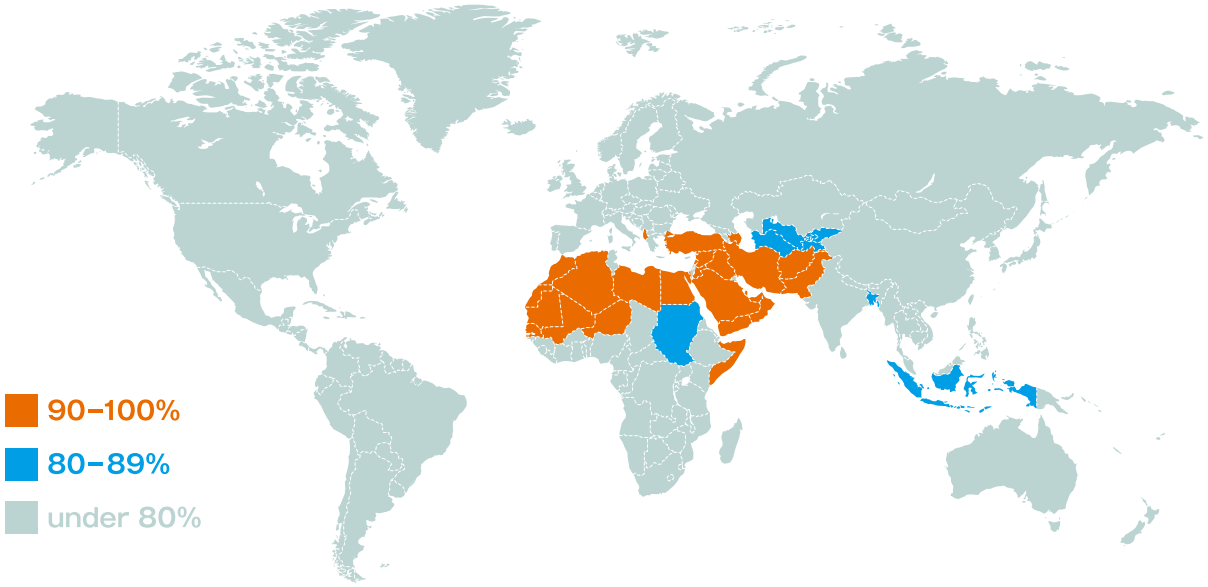
The major *halal* certifiers that approve foods, additive and other products made by Japanese corporations include LPPOM Majelis Ulama Indonesia (LPPOM MUI), Jabatan Kemajuan Islam Malaysia (JAKIM), the Islamic Food and Nutrition Council of America (IFANCA), the Japan Muslim Association (JMA) and the Japan Halal Association (JHA).

Exports to Islamic countries must undergo inspection by different halal certifiers according to the destination country. For example, as of January 2013, exports from Japan to Indonesia must be inspected by either MUI or JMA and exports to Malaysia must be inspected by either JAKIM, JMA or JHA. Therefore, Japanese corporations may need to receive approval from several *halal* certifiers in accordance to the requirements of the country where the goods are destined.

As the population of Muslim consumers increases, Japanese corporations will need to become more active in gaining *halal* certification. Amano Enzyme currently accepts *halal* inspections and is enthusiastically committed to complying with certification procedures to an even greater extent in order to satisfy our valued Muslim customers.

The Kobe Muslim Mosque

Countries in which Muslims represent more than 80% of the overall population



Amano Newsletter

Amano News Letter

Successful acquisition of Daiwa Kasei K.K.

On April 1, 2013, Amano Enzyme officially acquired Daiwa Kasei K.K.. Although Daiwa Kasei K.K. has been part of the Amano group since 2001, this official acquisition was consummated to strengthen our strategic position in an increasingly competitive market. Specializing in liquid cultures, Daiwa Kasei K.K. is the first Japanese firm to succeed in the industrial-scale production of α-amylase. The company will be converted into our production base in Shiga Prefecture.

Aerial view of the Shiga Plant
(former site of Daiwa Kasei K.K)

Construction of a new corporate building at Amano Enzyme USA (AEU)

Construction of the new corporate building is progressing at a fast pace at AEU.

Although delays were anticipated due to the unprecedented level of snowfall in Chicago this year, the building is expected to be completed on schedule. The new facility will be equipped with a blending plant to respond expeditiously to the ever-diversifying needs of our customers. Please look forward to services to be offered by AEU at the new building.

The new building under construction

News from Historical Archive of Enzymology in Nagoya

Part 1: The Enzymologist and the Violin

As reported in Volume 12 of Enzyme Wave, the Archive on the 6th floor of our head office opened as scheduled in June 2010. The first article of a series of News from our Historical Archive of Enzymology in Nagoya will describe how a couple of German scientists and a violin in Nagoya serendipitously crossed paths.

After the Meiji Restoration, Japan invited experts in various scientific fields from Western countries to help raise the national level of science and transform the country into a modern state. As part of this program, Aichi Medical School asked the renowned chemist and enzymologist Prof. Leonor Michaelis from Germany to come to teach a course of biochemistry newly set up for Michaelis in 1922. Michaelis arrived at the port of Kobe on December 1 of that year and headed directly for Nagoya.

By coincidence, around the same time, the famed theoretical physicist Albert Einstein had also arrived in Tokyo and travelled to Nagoya about a week after Michaelis. To celebrate their reunion in Japan, they held a concert at Michaelis's accommodations featuring Einstein on the violin and Michaelis on the piano.

On June 21, 2012, a local newspaper in Nagoya published a remarkable article written by Prof. Satsuki Inoue of the Aichi Prefectural University of Fine Arts and Music. According to this article, Mr. Shinichi Suzuki, who was the third son of Mr. Masakichi Suzuki, the founder of the Suzuki Violin Company in Nagoya, and who was also a famous violin instructor known for creating the Suzuki Method, got acquainted with Einstein when Shinichi was an exchange student in Germany; Michaelis introduced Shinichi to Einstein. When Mr. Suzuki returned temporarily to Japan and held a series of performances in various regions, Michaelis played the piano during his concert in Nagoya. Furthermore, Michaelis asked Einstein to evaluate four instruments specifically made for him by Masakichi. The letter dated November 2, 1926 from Einstein to Masakichi shows how Einstein highly rated his violins.

In 1926, James Sumner of the United States succeeded in crystallizing urease derived from jack beans and consequently demonstrated that the enzyme was in fact protein. However, Sumner's finding was met with opposition because the urease remained stable in the presence of proteases that usually broke down proteins. It took several more years of research to convince the scientific world that enzymes were composed of proteins. In June of 1926, Michaelis completed his tenure at Aichi Medical School and headed for the United States with his family.

Musically talented Michaelis began his tenure at Aichi Medical School in 1922. It was the same year that Mr. Genichi Amano, who was 17 years old at that time, started his local business to sell pharmaceuticals. Genichi would eventually go on to produce diastase as a medical product after world War II and expand small business into an international corporation.

There are a few enzyme manufacturers in Japan but three of them reside in Nagoya area. Behind the enzyme business lies the 90-year-old inspiring story of the enzymologist and the violin that is hidden in this very city.

From "Prof. Michaelis and Japan" edited by Kunio Yagi

Historical Archive of Enzymology

Amano Enzyme's Head Office can be reached by traveling east along Sakura-dori for about 1 km from the JR Nagoya Station. Although our Historical Archive of Enzymology is still small, we hope you will stop by when you are visiting Nagoya and browse through our list of materials. We also hope you will consider donating any resources on enzymes you might possess. We accept general publications, research paper compilations, academic theses and historical corporate documents. We look forward to your support in the future.

Historical Archive of Enzymology

- Location: Amano Enzyme Head Office, 6th Floor, 1-2-7 Nishiki, Naka-ku, Nagoya, 460-8630 Japan
- Open 9:00 a.m. to 5:00 p.m. (closed on weekends, national holidays and year-end and New Year holidays)
- Reservations required (contact us by fax at 052-211-3038 or by e-mail at library@amano-enzyme.ne.jp)

Amano Enzyme Message Board (June to December, 2013)

<Symposium>

Symposium on Enzyme Applications on June 14, 2013 in Nagoya Japan

This event will feature a talk by the winner of the Research Encouragement Prize as well as three corporate presentations and one special presentation. We hope you'll come to this symposium that will be full of exciting activities.

<Information on exhibitions>

We hope to see you at these exhibitions around the world. Come around and join us at our corporate booth!

2013.6.25~27	Shanghai, China	CPhI China
2013.7.14~16	Chicago, U.S.A.	IFT 2013
2013.8.6~8	Sao Paolo, Brazil	FI South America(FISA) 2013
2013.9.11~13	Bangkok, Thailand	Fi Asia 2013
2013.9.25~26	Mexico City, Mexico	Food Technology Summit & Expo 2013
2013.10.22~24	Frankfurt, Germany	CPhI-WW
2013.11.13	Chicago, U.S.A.	Chicago Section(CSIFT) Suppliers
2013.11.19~21	Frankfurt, Germany	FIE

Amano Newsletter

Amano News Letter

Report on exhibition participation last year

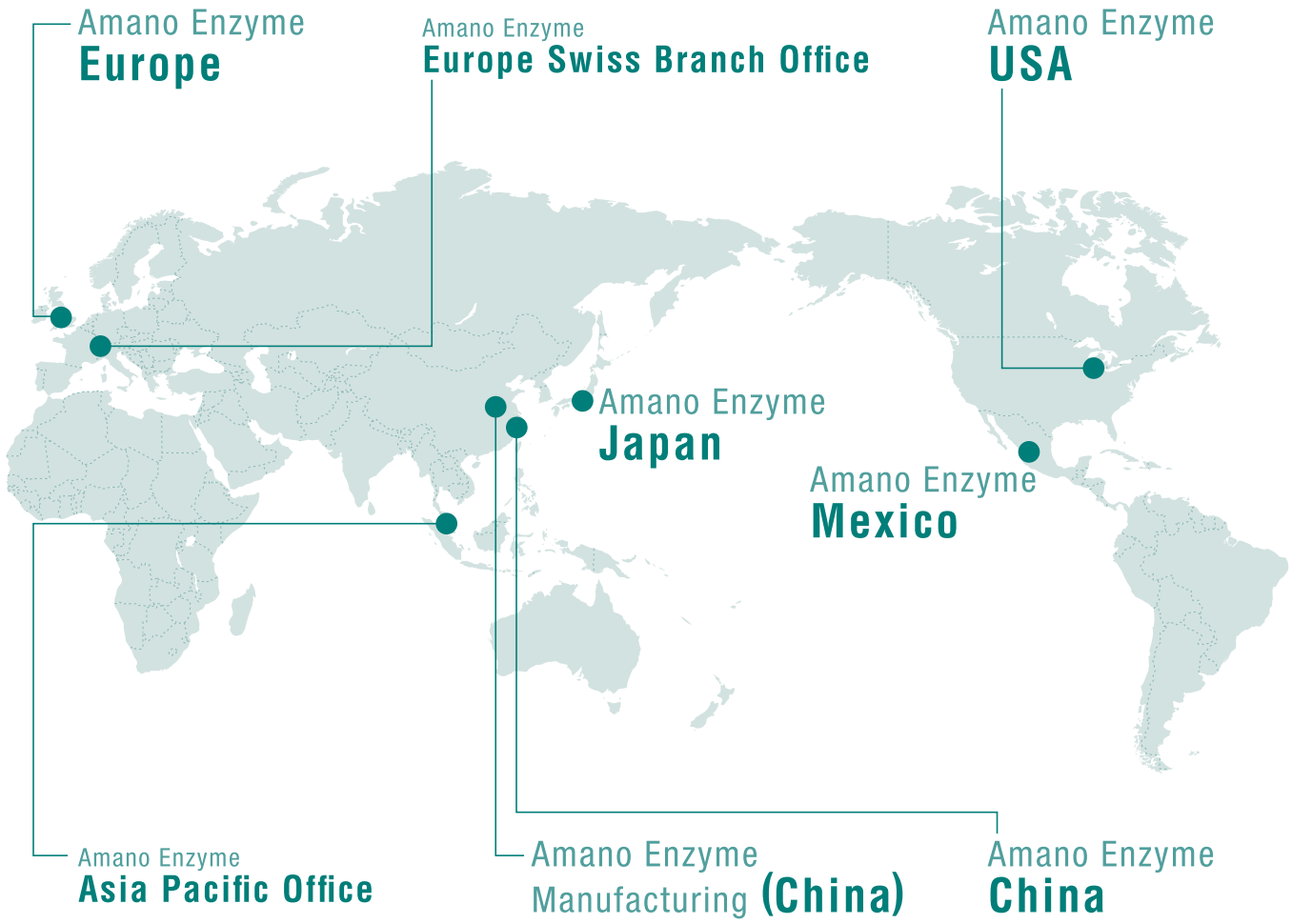
In 2012, we participated in food and pharmaceutical industry exhibitions in Japan, Brazil, Indonesia, Spain and the U.S.A. For the first time, we participated in events in South America (Brazil) and Southeast Asia (Indonesia), as part of our steadfast efforts to expand our marketing operations.

CPhI Madrid

Fi Asia 2012 Jakarta

Amano Enzyme

World Network



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