Biotechnology in Japan

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Japan takes biotechnology very seriously considering that the old biotechnologies such as fermentation, enzyme production, food additives and fermented foods have played a critical role in Japanese industry over the last century. Japan also has very strong markets for taking up the fruits of the new biotechnologies such as the pharmaceutical industry which is the second largest in the world, a large healthcare sector under strong pressure to reduce costs, a strong food processing industry hungry for new products and growing bioremediation and environmental sectors.

Changing the Paradigm

However, Japan believes that it is lagging behind in critical new biotechnologies such as recombinant DNA, genetic engineering and gene analysis and in the associated support industries for these areas. This concern has reached the very highest levels of government at a time when the country is facing change in a number of areas: the impact of a strong outward-looking China in the Asian region, continuing deflation in the economy, large government budget deficits and structural problems including weak competition in some sectors.

In the past, Japan had tried to select technologies and industries relevant to its future and had instituted bureaucracies to support this redirection. However, the government has realised that this paradigm has changed and at the turn of the century initiated mergers of government ministries to form super ministries in an attempt to provide more integrated and consistent approaches to change across government.

Significant changes for biotechnology were the decision to promote biotechnology with the establishment of a top level Biotechnology Strategy Council, the improvement of tax incentives to support research and development, the facilitation of clinical trials networks and a more overt acceptance of academics working with industry.

Current and Future Markets

In 2002, METI, the new super Ministry of Economy, Trade and Industry (METI) released the following information indicating the current market for new biotechnology products and what expectations were for growth over the next decade.

Japanese Biotechnology Market 2001/2010

(Units: ¥ x 10^9)

Sector	2001	2010	Required Annual Growth Rate
Human Health	536	8,400	36%
Agri-Food	367	6,300	37%
Bioprocess	244	3,600	35%
Environment & Resources	3	600	80%
Biotools	140	3,100	41%
Bioinformatics	29	2,200	62%
Services & Others	26	800	46%
Total	1,344	25,000	38%

Source: METI 2002

Unlike other Japanese industry, the new biotechnology industry, as distinct from the older fermentation and food additives industry, is almost entirely internally focussed with few exports and the following chart breaks down the industry into sectors with key products in each sector.

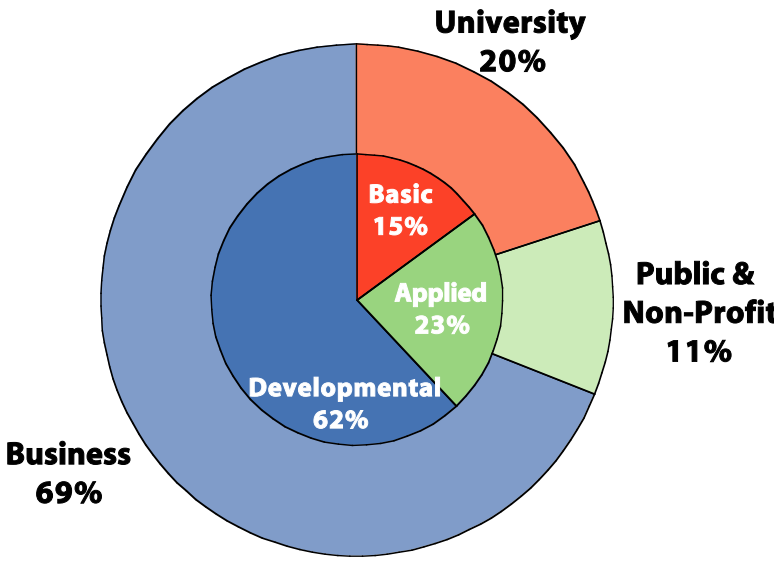
Biotechnology Market Key Sectors and Products

Sector	Share	Products
Human Health	40%	Erythropoietin (EPO), Granulocyte Colony Stimulating Factor (G-CSF), Monoclonal Antibodies, Growth Hormone, Insulin
Agrifood	27%	Maize, Functional Food, Special Health Foods
Bioprocess	18%	Enzymes for Food and Detergents
Biotools	10%	Biosensors, Analytical Equipment
Bioinformatics	2%	Complete cDNA cloning
Environment	-	Bioremediation
Services	2%	

Research and Development in Japan

Statistics on research and development expenditure in Japan in FY2002 indicate that ¥16,675 billion was spent on research and development, representing some 3.35% of GDP. Expenditure was split according to the following diagram and of this total amount, life sciences represents some 10%.

Research and Development Expenditure: Japan FY2002
¥16,675 billion



These statistics indicate that the major driver of biotechnology in Japan is business with some direction from Government and support from the University sector.

Government Direction

At top Government level, there is the Biotechnology Strategy Council comprising the Prime Minister, the Chief Cabinet Secretary, the Minister for Science and Technology Policy, the five key Ministers for Education, Agriculture, Industry, Health and Environment and 12 selected experts.

Below the Council, there are four government ministries with significant biotechnology-related budgets.

The Ministry of Economy, Trade and Industry (METI) deals with Japanese industry in the broad and has a modest biotechnology budget to support research institutions such as the National Institute of Advanced Industrial Science and Technology (NIAIST) and the National Institute of Bioscience and Human Technology (NIBHT). It also works with industry through intermediary bodies such as the Japan Bioindustry Association and the Research Association for Biotechnology.

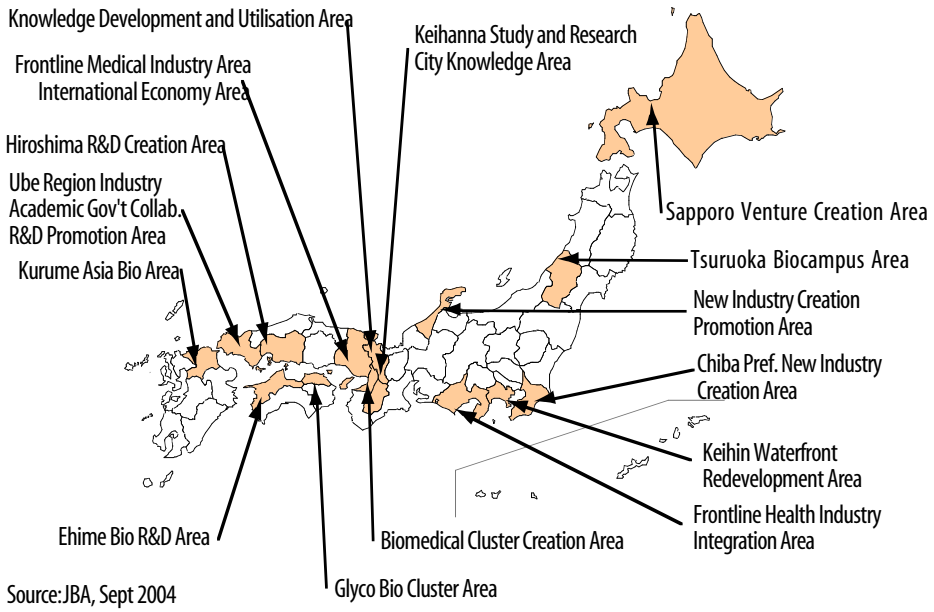
The Ministry of Education, Culture, Sports, Science and Technology (MEXT) regulates the university sector and has a substantial budget in support of biotechnology. It also supports a number of research institutions such as the Institute of Physical and Chemical Research (RIKEN) and the Research Organization of Information and Systems (ROIS) which was recently formed from the National Institute of Genetics, the National Polar Institute, the National Institute of Informatics and the Institute of Statistical Mathematics. Also in line with the government's desire to open the universities up to business, it has supported the establishment of some 43 Technology Licensing Organizations to promote the licensing of university-developed technology into industry.

The Ministry of Agriculture, Forestry and Fisheries (MAFF) has a relatively small biotechnology budget to support around 18 agricultural research institutes around Japan. However, it exerts significantly more control in the regulation of entry of agricultural products whether genetically modified grains or vaccines into the country in close consultation with agricultural cooperatives in Japan. It also works with industry through organizations like the Japan Society for Techno-innovation of Agriculture, Forestry and Fisheries.

The Ministry of Health Labour and Welfare (MHLW) has a significant budget associated with the support for development of pharmaceuticals, medical devices and diagnostics in Japan and also with regulation of products into the Japanese market. It collaborates with industry through the Japan Health Sciences Foundation.

Another driver which has developed in the last decade is local government at the prefectural level which is supporting the establishment of industrial clusters. By the end of 2004, some 42 bioclusters had been established with only those in the Tokyo, Osaka and Hokkaido regions having sufficient size to create synergy (see following graph). Local government also supports partnerships between local government and local business and funds regional institutes, particularly in the Osaka region where the Osaka prefectural government supports biotechnology because of the strong pharmaceutical industry there.

Structural Reorganisation of Special Areas

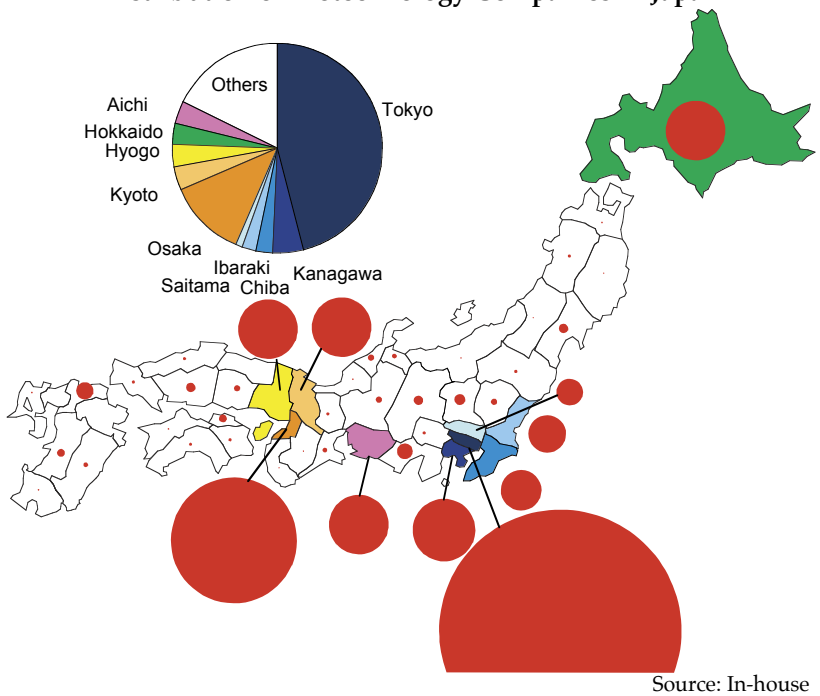


Source: JBA, Sept 2004

Japanese Companies: Distribution, Growth and Direction

Analysis of our in-house database of over 2,000 companies in biotechnology in Japan shows that biotechnology companies are clustered mainly in the Tokyo region then in the Osaka/Kyoto/Kobe (Hyogo) region with smaller numbers in the Hokkaido and Nagoya regions.

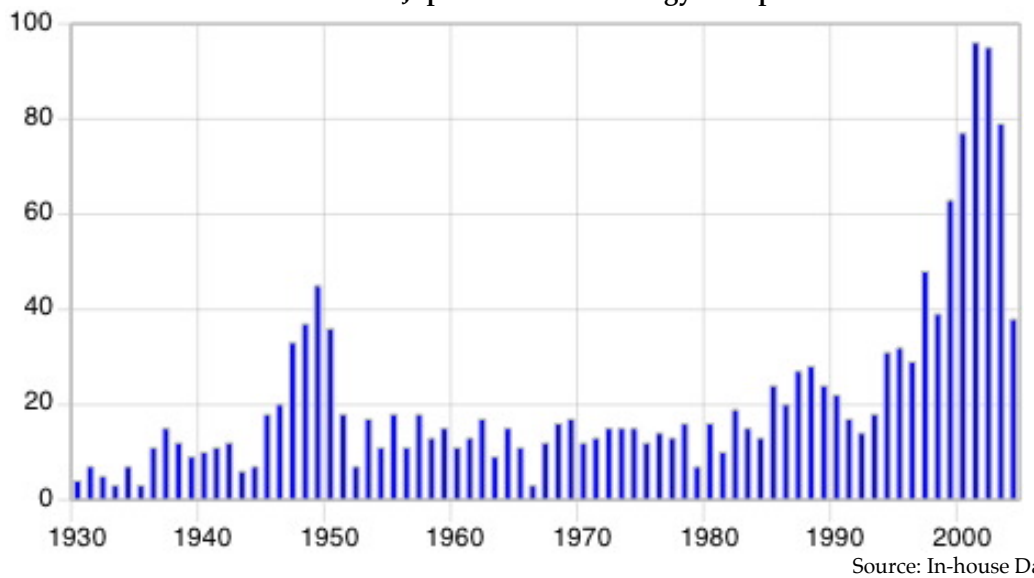
Distribution of Biotechnology Companies in Japan



Source: In-house Data

Furthermore, while there has been a constant establishment of biotechnology companies over the last 75 years in Japan, there have been three significant growth phases as indicated in the following graph: the post-war reconstruction period, the late 1980's when the new biotechnology was first promoted and then in the last few years when over fifty new companies have been established every year.

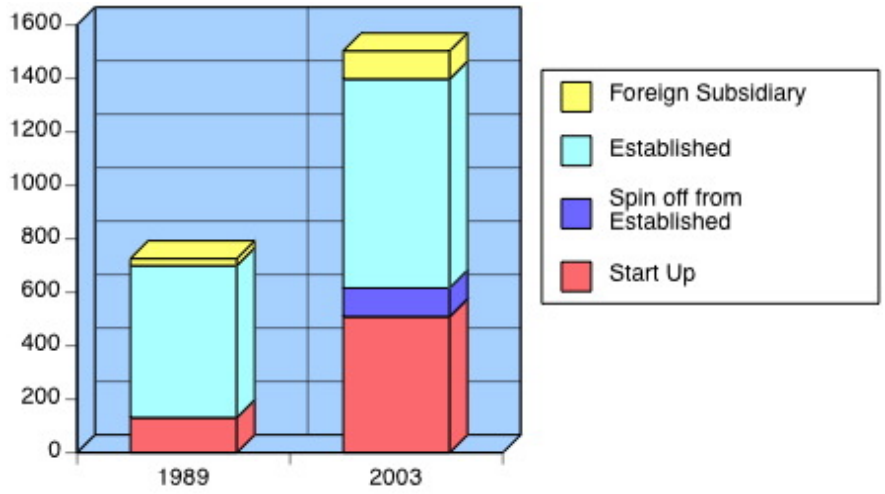
Establishment of Japanese Biotechnology Companies



Source: In-house Data

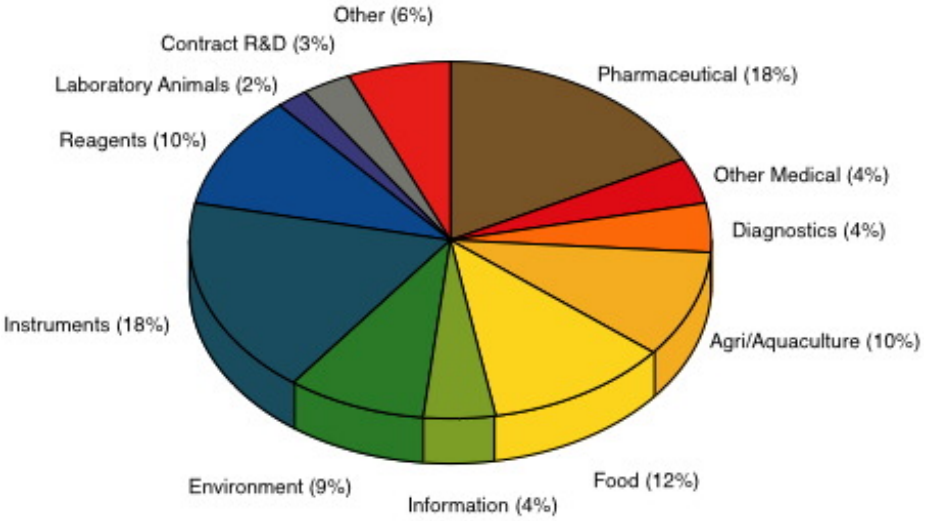
It is clear from the following graph that to a large extent established companies have moved into some new biotechnology areas, but in areas of less ready commercial exploitation, the established companies have supported spin offs or new ventures have been formed. These latter new ventures have suffered from the same problems as new biotechnology ventures have in other countries, namely lack of market interest and funding limitations.

Growth of Spin Offs and Start Ups



Our databases on Japanese companies indicate that about a quarter of Japanese biotechnology companies are in the health and medical sector covering pharmaceuticals, therapeutics and diagnostics, another quarter represents companies in instrumentation and laboratory support, 12% are in the food sector, 10% in agriculture/aquaculture and 9% in the environment sector (see below).

Sectoral Distribution of Japanese Biotechnology Companies



Areas of Opportunity

The area of most obvious opportunity for the biotechnology industry in Japan is the pharmaceutical sector. This market in Japan alone is enormous at around ¥6,000 billion with about 50% of the market controlled by local companies and a further 20% by local companies under foreign license. Because of the large number of companies in the sector, it is highly competitive and has been undergoing significant change in the last decade with further significant changes expected. With strong pressure to contain the health budget in Japan, there are limited local opportunities for expansion and many pharmaceutical companies are looking overseas to expand and survive. They are setting up operations mainly in the US and Europe to increase research and development and access new markets and are relying on increased sales in the Asia Pacific area for growth in the short term. Other companies may merge or disappear. New pharmaceutical companies which have been spun out of the food companies like Suntory have found it difficult to survive and in many cases are dropping out.

Another significant medical market in Japan is the medical devices market at around ¥3,000 billion, almost 60% of which is met by local companies, but there is significant importation of biomedical transplantation devices. There is also a keen interest by local developers in the application of tissue regeneration in this area as well as the development of biomaterials for use in transplantation.

The in vitro diagnostics market is another major user of biotechnology products and the market for these products in Japan is around ¥500 billion. While around 50% of immunoassay products are imported, the local instrumentation industry is strong in this area and competition for new products and processes is strong, driving further developments.

In agriculture, practical application of the new biotechnologies is relatively limited and confined mainly to the research institutions due to the protected nature of the local industry. There is significant interest in the application of biotechnology to genetically modifying commercially important crops and a number of GM crops have been tested. However, the market is becoming increasingly sensitive to genetically modified foods and this may hamper future developments in this area. A number of companies are looking to exploit biotechnology in the animal sector with the development of new vaccines and improved embryo manipulation techniques where Japan has a good reputation. However, here again market sensitivity is limiting the rate of development and introduction of new varieties. Future biotechnology developments in agriculture will be controlled by industry based on its strengths which are mainly in the seed industry with an emphasis on rice and vegetables. Corporate players are the pesticide, seed, beverage and brewing industries as well as the agricultural cooperatives.

The Japanese food and bioprocessing industry is a strong, highly competitive industry reliant to an extent on imported raw materials. It has been built on a long history of fermentation to produce food with adaptation to other industries rather than extension in existing industries. The strong market orientation of this industry has resulted in rapid adoption of new technologies to develop new and novel products and there is currently a strong emphasis in using biotechnology for the development of new special health or functional foods that fill a perceived gap between the food and pharmaceutical industries.

The Biotools market is a new area receiving significant government support, building on a strong electronics and laboratory equipment industry base in Japan. This sector is relying on an increase in local demand for growth and is being promoted through the push into nanotechnology firstly in electronics, then medical chemistry and finally into medical devices.

Bioinformatics is perceived in Japan as an area where it is falling behind other advanced countries and this has resulted in strong government support with the establishment of the Genomic Sciences Center in RIKEN, the establishment of the Helix Research Institute with government and industry funding and the adoption of a significant strategic patenting approach in the area.

The environment market in Japan is massive at ¥25 trillion and is growing annually at around 4%. The industry is highly competitive, particularly in industrial pollution control but there is increasing interest in applying biotechnology in wastewater treatment, soil and water remediation and associated services. It is expected that major future growth will be in soil and water remediation, pollution prevention services and energy saving and management and biotechnology could play a useful role in the adoption of new approaches.

Areas for Improvement

With industry controlling to a large extent the adoption and acceptance of biotechnology in Japan, it is left to the government related organizations to review regulations, support the development of new technologies for the future, pinpoint areas of weakness and promote collaboration between the industry and non-industry sectors.

There has been no shortage of discussion at the government and university level on some of the perceived limitations in Japan including:

- A lack of integration between academic research and industry, including the pharmaceutical industry
- A lack of bioventures in Japan resulting from shortcomings of the Japanese system including the lack of cooperation between government agencies, the lack of incentives to develop new technologies and commercialise them, the lack of translational research centres and a strict vertical system with an inflexible research structure that does not promote independence among young researchers.
- A complex and bureaucratic regulatory system in the health and agricultural/food sectors
- Limitations on the extent to which university academics can work with industry
- A perceived lag behind other countries in recombinant DNA research, gene analysis and diagnosis, genetic therapy, cancer medicines, drug delivery systems and bioremediation.

Initiatives and the Future

To a degree, the Japanese government has moved to address at least some of these issues. It invested ¥500 billion in life sciences research and development in 2002 and it supported the establishment of 43 Technology Licensing Organizations which promote the transfer of research achievements from universities to industry. Under this arrangement, activity costs of the organizations are partly supported, examination fees for licensing are exempted and small or medium sized businesses are entitled to receive some financial support when TLOs transfer licenses to them. Downstream from this, more than 1,000 venture companies based on technology developed by the university sector were established by April 2005 and many of these are in the biotechnology sector.

The support systems for bioventures have been improved with the integration of government ministries referred to at the beginning of this article and the establishment of a Biotechnology Strategy Council. However, historically Japan has not provided many incentives to support new technology development in companies and only recently moved to provide incentives in this area, more for small to medium enterprises than for large enterprises. The major promotion by government remains direct funding of research and development projects rather than the provision of tax incentives.

In the regulatory area, there has been a strong drive for change in the regulation of the pharmaceutical and medical device industry. The Japanese healthcare system, particularly the pharmaceuticals area, is undergoing major evolution with legislative changes to provide more consistency with regulatory processes used by US and European counterparts, while at the same time providing some protection against future weakening of the domestic pharmaceutical industry. Under the changes, some bureaucratic impediments will be removed for foreign companies interested in the Japanese market and there will be a stronger onus on local companies to provide a more active support system for the introduction of cheaper, more effective healthcare. Many issues remain to be resolved in the implementation of these regulatory changes and these will become more apparent as the legal changes are implemented.

Limitations on the extent to which academics can work in industry remain, although there is a strong will by the government sector to facilitate arrangements. In the past, national university professors were prohibited from concurrently holding the position of executive director in the private sector. Because of this, it was not possible for a university professor to transfer to a private enterprise together with the project he had been leading, to ensure that the industry could make the best use of the technology transfer. The impediment was mainly legal through interpretation of the National Public Service Law. As a result of the government's push to ease limitations on university industry interaction, and criticism by professors of these limitations, there has been a growing trend in recent years to take a more flexible approach to enabling university professors to work in industry.

In the area of perceived weaknesses in competition with other countries in the biotechnologies, the Japanese government, at the national and local level, can only play at the edges by funding projects and support certain technologies in the hope that eventually the more dominant industry sector will see an opportunity and adopt the technology.

One of these initiatives is Genome Bay, originally proposed by Dr Kenichi Arai, Dean of the Institute of Medical Science at Tokyo University (IMSUT), which plans to link genome research laboratories in the Tokyo waterfront area into a cooperative organization that combines business, academic and public sectors. The proposed participating centres include the University of Tokyo, the Kazusa DNA Research Institute, the Genomic Sciences Center of RIKEN in Yokohama, IMSUT and the Computational Biology Research Center (CBRC). Proposed supporting organizations include Mitsubishi Chemical, Mochida Pharmaceutical, the Tokyo metropolitan government, the University of Tokyo and the Tokyo Chamber of Commerce and Industry.

Another key initiative in the Osaka region has highlighted 11 biotechnology research projects for priority support by a panel composed of regional government representative, local businesses and others as part of a key desire by that area, the Kansai region, to become a major centre for biotechnology to support the pharmaceutical industry which is strong in that area.

Japan realises that biotechnology provides a number of opportunities for both its society and industry in the future and has started looking at ways of taking advantage of these opportunities at a time of significant change in the country and in the region. The fact that there is a Biotechnology Strategy Council chaired by the Prime Minister and containing leading ministers as well as eminent research and business representatives is ample evidence of this. How this Council works with the key areas of government, academia and industry will set the tone for the further development of biotechnology in Japan in coming years.

Dr Yukawa and Dr Venning have been working with the Australian biotechnology industry for over 30 years. Dr Yukawa graduated from University of Kyoto and University of New South Wales and following extended periods working for Biotechnology Australia Pty Ltd and CSL Ltd established his own company providing support to Australian companies accessing the Japanese market. Dr Venning graduated from Flinders University and the Australian National University and after working for government, large and small industry, established his own business assessing and valuing technology and other intangible assets for clients in the finance industry. Both are advisers to the Japan external trade organization, JETRO.