Japan - EU Workshop on Bioventures

- Report -

Tokyo, Japan
- 25 September 2000 -

Co-organised by:

MITI
- Ministry of International Trade and Industry -
  Basic Industries Bureau

And

European Commission
Research Directorate-General
Life Sciences Directorate

The report is available on the Internet at:
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EXECUTIVE SUMMARY

The European Commission Research Directorate-General and MITI - Ministry of International Trade in Industry - in Japan organised a joint EU-Japan workshop on bioventures - biotechnology start-ups and bio-entrepreneurship - on 25th September 2000 in Tokyo. This EU-Japan workshop was intended to be an opportunity to exchange information on the European and Japanese approaches to encourage biotech spin-offs - from universities but also from big firms -, entrepreneurial initiatives and new bioventures, as this is an objective of major importance both in Japan and Europe. This was the first opportunity for a direct exchange of experience on biotechnology between Japanese and European business people and scientists. Some mutual knowledge exists in Japan and the EU, however in the field of biotechnology, the general orientation has so far been towards USA. Japan and the EU are confronted to similar problems and face future challenges. Innovative reforms are being implemented to cope with these challenges and with the coming “Bio-Century”. They will have major impact on social and economic issues. The workshop demonstrated that ongoing initiatives such as TLOs -Technology Licensing Organisations-, bioincubators, new financial markets will contribute to the development of a modern biotech industry. Europe has managed this change at least with some success, and Japan shows signs for doing rapidly so. During the past four years, there has been explosive growth within the biotechnology industry in Europe. According to the last figures, Europe counts today some 1,351 specialised biotech companies. Although a more recent trend, growth of bioventures is also taking place in Japan which counts today 140 biotech firms.

The workshop provided an interesting and stimulating introduction to research and business in biotechnology in Japan and Europe. The opportunity to reflect together with European and Japanese policy-makers, business people, financiers and researchers on policy developments, different systems of start-up support and on the different investment climates was a very valuable one. Ingredients for success were identified – e.g. strong research and science base, entrepreneurship and cultural factors, management, IPR, Venture Capital – and are largely the same in Europe and in Japan. The difference is the recipe of the “chefs” to find out the most successful way to set up the virtuous circle of research, industry and finance stakeholders. It was considered important for this exchange of experience to continue and to deepen these discussions and contacts. In developing further the links between the Japanese and European biotechnology holders, the following opportunities are highlighted, and will be explored by the EC and MITI:

- Disseminate information in Japan on the third Conference of the European Biotech & Finance Forum, Cambridge, UK, 30Nov & 1Dec. 2000, which focus is on consolidation – new alliances, mergers, partnership between biotech firms.
- Organisation of a special event of the Biotech & Finance Forum dedicated to offering opportunities to showcase bioventures - based in Japan or Europe - and organise one-to-one meetings between Japanese and European prospective partners.
- Organisation of a special Europe-Japan symposium, within the 10th European Congress of Biotechnology - ECB 10 – on 8-12 July 2001 in Madrid, Spain. This symposium could include technical workshop on S&T areas of common interest, as well as bioventure presentations.
BioJapan 2000 is held from tomorrow, which is held in Asia in every 4 years. Many people from the committee and bioventure inside the EU are going to participate in. Japan-EU Workshop on Bioventures is held in this opportunity, and it is very meaningful to us to exchange opinions.

Bioindustry is the field that an expectation is being gathered as a leading industry of the 21st century with Information Technology as well in Japan. Big possibility moves greatly in various fields, like medicine, medical treatment, chemistry, the energy, and agriculture toward the realization. It has been swelling very much when expectation of the venture as players that shoulders it in Japan. It isn’t confined in the mere expectation, and the thing that says activities in this field of the venture is expanding rapidly as for the point of the actual performance as well.

There are two elements as that background as a thing that it is seen from the Ministry of International Trade and Industry, and it advances rapidly. First factor is that the distribution of the resources of the research and development toward this field that has been increased preponderantly and drastically for the last two years. The thing of Millennium Project has started by initiative of the former Prime Minister; Mr. Obuchi’s specially. This is the story from the beginning. There is actual condition that expands greatly even in the private sector respond to that a governmental research and development budget grows greatly, and it responds to in the university, the national laboratory.

The second element is a system reform proceeds greatly. Starting from the establishment of Technology License Organization (TLO) that transfers technology, which is buried in universities to industries. Moreover, institutional reform enabled university teachers getting positions of venture firms or private enterprises are permitted. Otherwise, government as before possessed all the qualification on patent application from the fruit of research and development by the government budget. At present, contracted companies are permitted to have the qualification on this kind of patent application.

Furthermore, through the reform of capital market, it became easier for the people of venture firms to get capital fund.

The Ministry of International Trade and Industry has proceeded with a series of system reforms said like this as an important part of the economic structure reform in this several years. In company with expanding of resources of research and development, and the system reform, venture firms in the biotechnology are expanding rapidly in Japan.

Finally, with sharing this movement with the people of EU, we would make an effort to realize possibility in this field as soon as possible with cooperating each other. I hope the working relations between Japan and EU becomes deeper on exchanging experience and information through the workshop.
PROGRAMME OVERVIEW

- **10:00 – 10:05: WELCOME SPEECH**
  - Japan: Mr. Iwao Okamoto, Director-General for Basic Industries Bureau, MITI

- **10:05 – 10:30: OPENING REMARKS BY THE 2 CO-CHAIRS**
  - Japan: Prof. Isao Karube, Member of Industrial Technology Council, MITI
  - Europe: Dr. Rainer Gerold, Director Life Sciences, DG Research / EC

- **10:30 – 11:30: OVERVIEW OF BIOTECH DEVELOPMENT IN JAPAN AND IN EUROPE**
  - Japan: Mr. Kazuo Katao, Director, Biochemical Industry Div. MITI
  - Europe: Dr. Philippe de Taxis du Poët, “Cell Factory” key action, DG Research / EC

- **11:30 – 12:30: BIO-ENTREPRENEURSHIP**
  - Japan: Dr. Koichi Sumikura, Research Centre for Advanced Science and Technology, The University of Tokyo
  - Europe: Dr. Werner Wolf, Special Partner TVM, Techno Venture Management, Germany + Prof. Donny Strosberg, Institut Cochin / CEO of Hybrigenics, France
  - Discussion

**LUNCH 12:30 – 14:00**

- **14:00 – 15:00: BIOVALLEYS AND BIOINCUBATORS**
  - Japan: Mr. Toshiro Okada, Deputy Executive Director, Dpt. of Planning, Chiba Prefectual Gov.
  - Europe: Dr. Jim Ryan, Director BioResearch Ireland + Mrs. Victoria Appelbe, AGIT mbH, Germany / Co-ordinator, INeurope Life Sciences Programme
  - Discussion

- **15:00 – 16:00: BIOVENTURE FIRMS**
  - Japan: Dr. Ryuichi Morishita, Associate Prof. Osaka University + Dr. Toshio Furuya, President & CEO, PharmaDesign, Inc
  - Europe: Dr. Carmen Vela, Managing Director, Ingenasa, Spain + Dr. Luis Amado, Executive Vice President, Biotecnol SA, Portugal
  - Discussion

- **16:00 – 17:00: BIOTECHNOLOGY INVESTMENT**
  - Japan: Dr. Yoshihiro Ohtaki, President, Biofrontier Partners, Special Adviser, Jafco Co., Ltd.
  - Europe: Mr. Georges Morris, Consultant, UK, + Mr. S.H. Hemmingsen, Investment manager, Danish Venture finance, Denmark
  - Discussion

- **17:00: CHAIRMEN’S CLOSING REMARKS AND END OF THE WORKSHOP**

- **17:30: RECEPTION**
EU
The Commission Research Directorate-General and MITI - Ministry of International Trade in Industry - in Japan are organising a joint EU-Japan workshop on bioventures - biotechnology start-ups and bio-entrepreneurship - on 25th September 2000 in Tokyo. This EU-Japan workshop is intended to be an opportunity to exchange information on the European and Japanese approaches to encourage biotech spin-offs - from universities but also from big firms -, entrepreneurial initiatives and new bioventures, as this is an objective of major importance both in Japan and Europe.

The European Commission has for almost 20 years been supporting the development of biotechnology in Europe, through a succession of research programmes, from small beginnings to the present programme “Quality of life and management of living resources”, with a budget of 2.4 billion Euro (1999-2002). However, we should remember that some 85% of Europe’s public expenditure on research are managed under the separate national authorities. Efforts at national level, effectively co-ordinated with one another and with the EU-level initiatives, are needed in the knowledge-based economy of the 21st century. This is the objective of the new Commission initiative for a “European Research Area”.

In the context of the "European Research Area", in particular the chapter on "Making Europe attractive to researchers from the rest of the world", the EU-Japan workshop is also aiming at highlighting to Japanese researchers, entrepreneurs and investors that Europe has become an attractive place for biotechnology entrepreneurship and bio-industries. All this new European landscape is not enough known nor visible enough in Japan, which is also implementing innovative plans to strongly encourage bioventure and bioentrepreneurship.

In both Europe and Japan, biotechnology first grew rapidly through the activities of large multinational companies in industrial sectors such as pharmaceutical, chemical, and food, but much less through start-up biotech firms. However, this quasi absence of start-ups and the predominance of large industrial groups have been perceived both in the EU and in Japan as a weakness. Although large corporations are still playing a major role in our economic systems, the research-based small companies are considered dynamic, focused, innovative, flexible, and rapid to both produce research results and exploit them, therefore having a competitive advantage, which is underexploited in Japan and in Europe.

The EU and Japan are confronted to similar future challenges. Innovative reforms are being implemented to cope with these challenges and with the coming “Bio-Century”, as MITI says. They will have major impact on social and economic issues. It is therefore needed to head towards more knowledge and understanding between the EU and Japan, in order to learn and benefit from it, avoiding a defensive or passive attitude, and promoting a constructive one. Along this line, ongoing initiatives such as the EU-Japan Forum on science & technology, 22-23 June 2000, Lisbon, Portugal, and the EC-MITI Biotech policy working group are useful contributions. In this context, the EU-Japan workshop on bioventures is an excellent opportunity to go further into this information and learning process.
A final point concerns the synergy between the EU-Japan workshop on bioventures and the “BioJapan 2000 International Conference, in Tokyo, organised by JBA – Japan Bioindustry Association, which is organised takes place just the days after the workshop. In addition, the visit of the bioincubator “Kasuka Academia Park” in Chiba prefecture on 26 September can only reinforce further contacts between researchers, entrepreneurs and investors from the EU and Japan.

Dr. Rainer Gerold, Director Life Sciences  
European Commission, Research Directorate-General

Japan
Since the 1980s, the importance of research in the area of biotechnology has been highlighted in Japan. In Japan, however, neither the government nor the companies have been able to invest on research and development (R&D) in this field and bring venture business up. It is important for Japan to reflect on this.

On the other hand, western countries have succeeded in promoting industries for biotechnology. Particularly, the USA has concentrated its efforts on doing so by means of a strategic policy attributed to the Bayh-Dole Act, which was enacted in 1980, as well as an enormous financial investment on R&D. Under the law, universities have established liaison offices and technology licensing organizations (TLOs) and licensed the research results as patents for technology transfer to companies. Approximately 1,900 venture companies had been set up by 1996. Furthermore, these companies had 0.22 million employees and a market amounting to 3.7 trillion yen in 1996.

At present, the mismatch between research carried out at Japanese universities and company requirements is obvious. However, the creation of original technologies should be possible in the future, when the results obtained at universities are successfully transferred to companies as successfully as in the USA. Further, it is expected that many creative venture companies will be developed by the activation of Japanese industries.

The Japanese government enacted a technology transfer law in 1998, which enabled universities to establish TLOs. At the University of Tokyo, the Center for Advanced Science and Technology Incubation, Ltd. (CASTI) was established by the investment of staff members on the university. CASTI was acknowledged by the Ministry of Education, Science, Sports, and Culture and the Ministry of International Trade and Industry (MITI) as the first TLO in Japan. Researchers of other universities or national laboratories can utilize CASTI freely. In order to obtain fees for patent applications and personnel for running CASTI, membership fees are collected. CASTI member companies are able to obtain the contents of patents released within 14 days as well as priority rights for negotiations.

With the establishment of companies for technology transfer, faculties of universities have also become interested in the intellectual property of patents. In particular, platform-type patents, which extend the right to a patent, are becoming increasingly popular among the faculties due to the counseling of patent attorneys. Because of such activity of universities, industries tend to be interested in the value of the intellectual
properties owned by universities. So far, Japanese companies have not always paid researchers for the value of their research and knowledge. Therefore, TLO has been playing a significant role in bridging the gap between companies and researchers.

CASTI is currently trying to identify technologies, which had been hoarded in laboratories for a long time to apply them as patents. The Center for Collaborative Research (CCR), which assists CASTI in identifying possible patents, is in charge of storing this knowledge for the transfer of technology to companies. As a result, CASTI has succeeded in transferring several technologies and contributed to starting venture companies.

Twenty years after the success of the USA, Japan could establish a system for technology transfer to companies by licensing the results, which have been stored at universities, as patents. Such a system would be the answer to the plight of even small companies requiring this technology transfer. At present, a total of sixteen universities have established their TLOs, and a council of TLOs will be established. The number of such universities is increasing, and inquiries have been flooding the TLOs. On the other hand, the universities will have a significant role in their contribution to companies in addition to education.

The Japanese economy is going from high to low economic growth, whereas developing countries are catching up with the Japanese economy. Therefore, for the advancement of the Japanese economy, the creation of original technologies will be essential. In the future, venture companies which make good use of fundamental research or technologies in universities or create original technologies will be able to survive.

Prof. Isao KARUBE, Director of Center for Collaborative Research (CCR)
The University of Tokyo

(Slides of MM Gerold and Karube in annex 1)
Biotechnology is recognised as an essential issue for industrial development, growth, quality of life and employment in Europe. The acceleration of the progress of knowledge and the rhythm of important discoveries represent a genuine challenge to our capacity to exploit them. Another aspect is the continuous shortening of the time lapse separating a discovery from its commercial use, stressing the emergence of a more integrated rather than sequential innovation process, combining stakeholders from biotechnology research, industry and finance, and focusing on entrepreneurial activities and research-based start-up firms.

At the economic and industrial levels, there is certainly a message of hope for Europe. According to the last figures, Europe counts today some 1,351 specialised biotech companies. They employ directly almost 53,000 persons, generate incomes of about 5.4 billion Euros and invest 3.2 billion Euros in research and development. During the past four years, there has been explosive growth within the biotechnology industry in Europe – 131% growth in the number of firms, 211% growth in the number of employees, 264% growth in revenues and 152% growth in R&D expenses. The nurturing environment that helped foster this growth is essential for continued development. With new alliances, mergers and partnerships between biotech firms, this environment should be reinforced. By promoting and facilitating consolidation in the biotech sector in Europe, the virtuous circle of research, industry and finance holders will lead to more competitive firms, and a new generation of bioentrepreneurs to start up and flourish.

A series of factors at regional, national and European levels has contributed to improving the European situation and giving rise to a new positive mood in biotechnology. Without pretending to mention all of them, here are 3 general observations:

- The creation of new European stock markets for high-growth companies (e.g. EASDAQ, Euro-NM) has reflected the development of a new state of mind among the specialists in the financing of innovation in Europe. It starts to have positive effects.
- There is increased awareness of biotech stakeholders that small biotech research firms correspond to a reservoir of industrial competitiveness, scientific and technological innovation, opportunities for investors, and job creation, still underexploited in Europe. For example, the German initiative “BioRegio” has helped to mobilise and co-ordinate the efforts in a country which was previously far from exploiting its full potential.
- The promotion of an entrepreneurship culture through education and training in universities, enterprise incubators, biopoles, etc. has prepared the grounds for a new generation of entrepreneurs to start-up and flourish. These entrepreneurs have been trained to combine excellent research with other issues such as intellectual property rights, business management and interactions with investors.

Europe has an outstanding record of achievements in Life Sciences and Technologies research and the European Union research programmes have clearly demonstrated the
benefits that can be achieved when the best of European researchers work together in collaborative programmes. Building on the successes of the 4th Framework Programme but learning from our past experience, the 5th Framework Programme represents a radical departure from the traditional approach, as the programme focuses on societal needs. In line with the topic of this EU-Japan workshop on bioventures, the socio-economic objective and problem solving approach of the “Cell Factory” key action, one of the 6 key actions under the theme “Quality of Life and Management of Living Resources” give particular attention to strengthening knowledge-based young industries and linking the ability to discover to the ability to exploit. Other Commission initiatives such as the “Biotechnology & Finance Forum” launched with EASD will contribute to mobilise European players from research, industry and finance sectors.

Europe has to become a major place for producing and exploiting knowledge in the field of life science and technology. As for the other main priorities of the 5th Framework Programme, this materialisation of the results of research is essential so that the research of the 21st century is truly at the European citizen’s service.

Dr. Philippe de Taxis du Poët, Cell Factory Key Action, Life Sciences Directorate
European Commission, Research Directorate-General

Japan
I would like to explain Japanese government policy, particularly MITI’s policy that what kind of policy is taken in this 2-3 years, and what it will try to do from now on.

Biotechnology as a Strategic Industry
When you say a goal about the biotechnology of the Japanese Government with the word, it is that we are going to raise biotechnology as a strategic industry, as well as the information technology in the 21st century. It is a goal for a maximum to say that technology promotion is placed on main stream in the governmental policy. It was one of reflection to say that there was a lack of the power in this field for the last 10 years from the government surveys.

The MOU by 5 Ministers
First of all, it agreed on the policy toward the creation of the bioindustry by five Ministries from Science and Technology Agency, Ministry of Education, Ministry of Welfare, Ministry of Agriculture, and MITI in January 1999. It is called as the MOU by 5 Ministers. Six months latter, each ministry drew up the basic strategy in July 1999.

Under the MOU, a concrete goal for achievement in five years is shown. This may be summed up in the following few words. In the first, putting the ground for development of technology and making it a lever for promotion of industry. As the second issue, though there is various governmental research and development budgets, it is made to shift toward the realization. The third one is the environment maintenance. The fourth is the safety matter.

As the contents of the putting basic ground, there is a genome analysis in the first. We don’t have the intention to compete with Celera Genomics on the same ground as our approach. This is that the technology, which Japan has individual advantage to, be
taken out and intensive investment, is done. Though this project has started since this year, it has been going smoothly until now.

Not only human genome but also other field that relates a microorganism, a plant, especially rice, a genetic analysis related to others livestock are also proceeded parallel. Moreover, the field of bioinformatics is taken seriously as a future field that becomes in the center of the function analysis.

Budget for 2001
At present, a budget requirement time of 2001 is proceeding. There is a total budget of 82 billion in this year. 5 Ministries will put 120 billion-yen for the next year, this is 50% increasing compared to this year’s budget, and it is required. Big flow comes out not only the inside of the government but also the legislatures respond to our movement. The government ruling party established the life science member league. And, as for the private side as well, the biotechnology Session was established in the Federation of Economic Organizations last October.

Technology Licensing Organization (TLO)
Regarding the other conditions, a Technology Licensing Organization (TLO) was established to encourage the patenting of university research and facilitate the distribution of this intellectual property to the industrial sector. 16 TLO have already been established in Japan.

Investment Fund
Concerning the finance, the budget of a little over matching fund 14 billion yen was prepared with the government last year, and investment toward the venture enterprise was done when the fund of the private side was fitted to this. Moreover, on the private sector, Mothers that is a new security exchange market for venture firms is established in the Tokyo Stock Exchange, and the NASDAQ Japan is established in Osaka Stock Exchange as well. Moreover, the movement of establishing new venture capital comes out from the private, and venture fund technically to invest in biotechnology field appears 7 or 8.

The Special Measure Law
Furthermore, the Special Measure Law that enables to transfer the fruit from the governmental research and development to the industry was enacted.

Bioventure Firms
As a result of above elements, more than 140 bioventure firms are active at present. There was only about 60 companies 2 years ago. I would like to promote the thickness of Japanese bioventure with raising the function itself. Thank you for your kind attention.

Mr. Kazuo KATAO, Director, Biochemical Industry Div. MITI

(Slides of MM Katao and de Taxis du Poët in annex 1)
JAPAN AND EU PRESENTATIONS
- Bio-entrepreneurship –
MM WOLF AND STROSBERG (EU) AND SUMIKURA (JAPAN)

Summary

EU
Entrepreneurship is defined as the organisation, management, and assumption of risks of a business or enterprise, usually implying an element of change or challenge and a new opportunity. Training should prepare entrepreneurs – personal qualities and attitudes, adaptive skills, specific knowledge - for the challenges of start-ups. Internal reasons for failures are essentially related to a lack of focus on main objectives, under-capitalisation or poor management of human and/or financial resources. Effective management of IPR is more crucial in the biotech sector than anywhere else.

The business plan – crucial to attract investors – must be considered in a very early stage of an entrepreneurial initiative. In short management, science and capital are the 3 main ingredients of supportive environment for bio-entrepreneurship. The main message was that the attitude towards entrepreneurship is improving in Europe and undoubtedly developing, but it needs still to be promoted, in particular in the universities. Finally, both entrepreneurs - start-ups from academic research -, and “intrapreneurs” - spin-off from large companies – can set up successful bioventures.

Prof. Donny Strosberg, Institut Cochin / CEO of Hybrigenics, France
Dr. Werner Wolf, Special Partner TVM, Techno Venture Management, Germany

Japan
In this paper I review what happened in US when genetic engineering industry was formed in the period from late-1970’s to early-1980’s, based on which the conditions required for the formation of biotech-related novel industries in Japan are discussed. Here I examine the formation process of genetic engineering industry in US by dividing the process into two stages, the formation of Genentech and its success, and the formation of other companies inspired by Genentech’s achievements.

(1) The commercial research of genetic engineering had not been performed until Genentech was formed in 1976 to produce useful proteins in E. coli. The key to Genentech’s success was its business plan, which was drafted as the collaborative work of entrepreneur Swanson and molecular biologist Boyer. What required for Japan today is establishment of an infrastructure to facilitate adequate matching of entrepreneurs and scientists. One candidate for such an infrastructure is Technology Licensing Offices, recently being formed to intermediate between university inventions and industrial corporations.

(2) As a condition under which a large number of venture companies inspired by accomplishments of Genentech could be formed, we should not think little of the presence of large human resources, including science-minded entrepreneurs and investors, and business-minded scientists. It is necessary to build up the similar human resources in Japan today. The recent amendment of regulations in Japan facilitate a professor in national universities to start up a company based on their research accomplishments and to be director of the company, which is supposed
to contribute to increase the number of business-minded professors. A person who has science background and is seeking for learning business matters should be supported financially to increase the number of science-oriented entrepreneurs or investors.

In the last section of this paper I briefly report the activity of “The Study Group For Intellectual Property Management”, which I am organizing for young biotech researchers who are interested in IP management or venture formation.

*Koichi Sumikura, Research Center for Advanced Science and Technology*  
*The University of Tokyo*

(slides of MM Sumikura, Strosberg and Wolf in annex 1)
The concept of a BioValley is a region or state that has put together the different components required to develop a successful bio-industry. The essential components are seen to be:
- A source of biotechnology expertise and research
- An industry base which is appropriate for adoption or support of biotech
- The funding, skills, infrastructure linkages and industry support to ensure that technology is developed, transferred and commercialised.

To create a BioValley, there must be public and political support for the establishment of the necessary components. In the example of Ireland, early effort went into investment in R&D and in creation of a Tech-transfer mechanism (BioResearch Ireland). More recently, the emphasis has been on further development of elements of support for the industry base (seed-funding, management & entrepreneur training etc). In summary, a biovalley is a dynamic system with many components all of which require attention in order to develop a successful bio-industry base.

The Euregio Meuse-Rhine is a “biovalley” in Europe in which three regions in three countries (Belgium, Germany and The Netherlands) have begun a close cooperation in the field of life sciences in response to rapid growth in this sector. By strengthening cross-border business activities and cross-border research co-operation and by marketing the Euregio Meuse-Rhine jointly as one region, the partners aims to promote synergies between their regions and to achieve the necessary critical mass required in order to compete globally. Services are provided to investors, companies and starters through the common network “Ineurope”, and innovative provision (and financing) of infrastructure for young biotechnology firms has been developed, so that the cluster will be able to grow quickly.

It was concluded that fostering collaboration, even among European regions which are highly disparate, is certainly worthwhile and that it is important to set ambitious goals for the promotion of biotechnology research and entrepreneurship.

**Dr. Jim Ryan, Director BioResearch Ireland**

Mrs Victoria Appelbe, AGIT mbH, Germany / Co-ordinator, Ineurope Life Sciences Programme

**Japan**

1. Introduction of Kazusa Akademia Park

Kazusa Akademia Park is the development project, which focuses on the establishment of core for research and development (so-called Research Park) reflecting the important location of Kazusa Area as traffic conjunction and the possibility of human-nature coexistence in Kazusa Area.

2. Basic Concept of Kazusa Akademia Park (decided in June of 1984)

Establishment of Research and Development Center Research and Development Facilities mainly by the private sector should be intensively located in order to
establish new business core area located in Tokyo Metropolitan region and improve
the position for higher value added Industrial Sectors in Chiba Prefecture.
- Establishment of Academic Center: Universities and Research Institutions with
  specialty, which could attract research and development facilities of the private
  sector by offering scientific information, opportunity for interactive research
  activity and human interface, should be located.
- Establishment of Production Facility: In the case that high-tech industry would
  like to establish production facility as well as research and development facility,
  they should be established in package.
- Gradual Development of the Project: Development should be implemented
  gradually. The first development cluster should be developed as composite of
  central facility utilized for research cluster, and research institutions.

3. History of the Development of Kazusa Akademia Park
- Project Plan of the first development cluster was decided in January of 1987. The
  method of development was decided to be “rezoning”.
- The implementation of the plan, namely, rezoning process started in March of
- Kazusa Akademia Park Co., LTD. was established in June of 1991 in order to
  operate the central facility utilized for research cluster and manage the Kazusa
  Akademia Park as a whole.
- Kazusa DNA Research Institute started its activity in October of 1994. The
  explanation about this institute will be given later.
- Major structure of the first development cluster was completed in March of 1996.
- Construction of the central facility utilized for research cluster, namely, core
  function such as convention hall, hotel, commercial facility and recreation facility,
  in the first development cluster area was completed and the operation started in
  February of 1997.
- In March of 1998, then Tokyo Tanabe Pharmaceutical, current Mitsubishi Tokyo
  Pharmaceutical, opened its laboratory in Kazusa Akademia Park.
- Biological Resource Center will start its operation in the spring of 2002.

4. Activities for Venture Business Support
- Construction of Business Incubator Building: In April of 1999, Kazusa Incubation
  Center, which has eight laboratories, started its operation. In October of this year,
  Creation Core Kazusa, which is supposed to have five laboratories and eight
  offices, will begin its operation.
- In Kazusa Incubation Center, five companies and two institutions are now running
  their business.
- Improvement of Venture Business Support Facility: Currently, improvement of
  venture business support facility, namely, establishment of support mechanism
  with human aspects, is undertaken. This improvement includes two major aspects.
  One is management support by human involvement and network, which intends to
  provide venture companies with "mentor facility", enhancement of managerial
  resource and capability, opportunity for networking, and opportunity for matching
  between venture business and financial agency such as Venture Capital and
  Angel. The other is liaison activity, which intends to increase opportunity for
  venture business formation by properly mediating "seeds" from academic arena
  and "needs" from business arena and market place.
5. Issues to be dealt with
In Research Park of developed countries, it is usual to activate research and development activities of private sector by taking advantage of already-established academic and research function. On the other hand, in the development of Kazusa Academia Park, all of research and development facility including academic related part was intended to be established from the scratch.
In Kazusa Akademia Park, Kazusa DNA Research Institute, as pioneer, has already established its reputation. Besides, additional academic institutions should be located because they play very important role both in attracting research and development institutions of private sector and in creating venture business activity.
In addition, we have to attract attention from business arena by presenting strategic plan for the future of the Park, and establishing human and information network.

Toshio OKADA, Deputy Executive Director, Dpt. Of Planning
CHIBA Prefectual Government

(slides of MMOkada, Ryan and Mrs Appelbe in annex 1)
**JAPAN AND EU PRESENTATIONS**  
- **Bioventure firms** –  
  **MRS VELA AND MR. AMADO (EU) AND MM MORISHITA AND FURUYA (JAPAN)**  

**Summary**

**EU**  
INGENASA - “Inmunologia y Genetica Aplicada SA” - was created in 1981, as a company devoted to the industrial applications of biotechnology. The aim is to develop and commercialise products for the diagnosis and prevention of infectious diseases of relevant economical interest in Animal Health. Ingenesa has developed the technologies and assembled the human resources necessary to face this challenge, combining multidisciplinary teams in immunology, molecular biology, genetics, as well as using monoclonal antibody technology, cloning and sequencing of nucleic acids, protein expression in micro-organisms, PCR, etc. Ingenasa has a full catalogue of more than 50 diagnostic product, and a new vaccine technology, reaching a world leadership in some of them. These results would have not been possible without a fruitful collaboration with public and private, national and foreign institutions. In the future, Ingenasa will reinforce its commitment towards international focus and search for innovative solutions to disease problems, using new technology to contribute to improving animal health world-wide.

BIOTECNOL is a research based biotechnology company. Founded in 1997, it has been at the forefront of biotechnology in Portugal and was a target for a first round of investment in late December 1999. The Company has built a technology platform based on novel approaches for recombinant protein expression in the bacterium Escherichia coli (*E. coli*). Biotecnol is now broadening its expression technology, by setting up R&D collaborations with academic research groups and companies in order to offer recombinant protein expression and production in various types of yeast and eventually animal cells, so that several systems can be assessed to determine the optimal process for production of any protein. Biotecnol has an innovative way of approaching process and product development. We prototype optimal and high-yielding processes for production of recombinant proteins and plasmid DNA, using state of the art technology. From the very early stages of our cost-efficient process development, we deliver a full documentation according to the current regulatory guidelines. That is applicable for all stages, ranging from the cloning process to quality control. Furthermore we take the process to GMP production standards by out-sourcing capacity at well-established Contract Manufacturers in order to deliver clinical grade batches, together with the necessary documentation for registration through the EMEA Centralised Procedure.

For both firms, the right “cocktail” for success is based on highly innovative proprietary technology with low risk development, large markets targeted, and a top scientific quality of research network. However the attitude of manager is crucial. She/he must be able to build up a team with strong awareness of the needs of the others, constituting a group of collaborators better than herself/himself. Her/his long term vision will be crucial. The difference between a successful manager and others is not a lack of strength, nor a lack of knowledge, but rather a lack of will.

*Dr. Carmen Vela, Managing Director, Ingenasa, Spain*  
*Dr. Luis Amado, Executive Vice President, Biotecnol SA, Portugal*
**Japan**

*Adventure in Gene Therapy: MedGene - as the First Academic Genetic Bioventure.*

Gene therapy is emerging as a potential strategy for the treatment of cardiovascular disease such as peripheral arterial disease, restenosis after angioplasty, vascular bypass graft occlusion, transplant coronary vasculopathy, myocardial infarction, for which no known effective therapy exists. Some aspects of the biology and pathophysiology of the cardiovascular system start to emerge, and then the time is ripe for the introduction of gene therapy to the management of cardiovascular disorders. Recently, the efficacy of therapeutic angiogenesis using VEGF (vascular endothelial growth factor) gene transfer has been reported in human patients with critical limb ischemia and myocardial ischemia.

Thus, the strategy for therapeutic angiogenesis using angiogenic growth factors should be considered for the treatment of patients with critical limb ischemia or myocardial infarction. From this viewpoint, we focused on a novel angiogenic growth factor, HGF (hepatocyte growth factor). Although HGF is originally identified as a most potent mitogen for hepatocytes, we found the potent angiogenic property of HGF in rabbit hindlimb model. According to this unique character, we plan human clinical trial to treat peripheral arterial disease using HGF. The clinical utility of HGF may be expanded to treat myocardial ischemic disease and cerebrovascular disease.

On the other hand, we developed cis-element double stranded (ds) oligodeoxynucleotides (ODN) (= decoy) as a powerful tool in a new class of anti-gene strategies for gene therapy. Transfection of ds ODN corresponding to cis sequence will result in the attenuation of authentic cis-trans interaction, leading to the removal of trans-factors from the endogenous cis-elements with subsequent modulation of gene expression. This 'decoy' strategy is not only a novel strategy for gene therapy as an anti-gene strategy, but also a powerful tool for the study of endogenous gene regulation in vivo as well as in vitro.

The transcription factor, NFkB, has been reported to up-regulate these cytokines and adhesion molecules such as VCAM and ICAM. Thus, we identified NFkB as an ideal target for inflammatory disease. Our data demonstrated the efficacy of NFkB decoy to treat restenosis after angioplasty, myocardial infarction, glomerulonephritis, arthritis and cancer metastasis. In this year, we will start phase I trial using NFkB decoy to treat restenosis after angioplasty.

For transfection of therapeutic genes, we also developed the viral (HVJ)-envelope with liposome method (HVJ-liposome method). Our numerous data documented the superiority of HVJ-liposome method in transfection efficiency into many organs including heart and blood vessels. MedGene BioScience Inc. is currently developing the unique gene-based medicine such as HGF and NFkB decoy in Japan and other countries.

*Dr. Ryuichi Morishita, Division of Gene Therapy Science*  
*Osaka University Medical School*

**PharmaDesign Inc, the First Japanese genome-based drug discovery company**  
PharmaDesign Inc (http://www.pharmadesign.co.jp/) was founded as a first genome-based drug discovery company on January 25, 1999, by Drs. Toshio Furuuya, Yo Matsuo and Teruhisa Noguchi. PharmaDesign is a drug discovery service company.
which has close contact with pharmaceutical and biotech companies, and also deals in unique bioinformatics solutions product, Biopendium™ which was developed by UK bioventure, Inpharmatica. In addition to these business PharmaDesign has undertaken to identify and validate of various drug targets for drug discovery from the data of genome sequencing projects and SNPs data.

Dr. Toshio Furuya, President & CEO of PharmaDesign Inc / Visiting Professor, Institute of Molecular and Cellular Biosciences, The University of Tokyo

(Slides of MM Morishita, Furuya, Amado and Mrs Vela in annex 1)
EU

Venture capital is management and money invested by professionals in young enterprises that have significant growth potential and may become significant contributors. The biotech investment professionals, in their quest for investment opportunities, will focus on and be attracted to regions that meet certain criteria, notably:
- Strong research & technology infrastructure comprising universities, university hospitals, technological service centers and specialized CRO’s.
- Public support schemes (financial and consultancy) to innovators/entrepreneurs and emerging ventures.
- Positive attitude towards biotechnology in the general public.
- Presence of well established pharmaceutical companies who constitute potential customers, sources of senior biotech management and spin offs.
- A political climate and fiscal system that allows entrepreneurs to become rich (“economically independent”) if their endeavors are successful and a culture that accepts failures as valuable experience.

As an illustrative example, Medicon Valley, a region consisting of greater Copenhagen and South Sweden meets these criteria to a high extent as is clearly demonstrated by an almost 10 fold increase, over the last 5 years, of venture capital dedicated to investments in biotechnology ventures.

Mr Georges Morris, Consultant, UK
Mr. S.H. Hemmingsen, Investment manager, Danish Venture finance, Denmark (now at Dansk Erhvervsinvestering A/S)

Japan

Apologies from Dr. Yoshihiro Ohtaki, President, Biofrontier Partners / Special Adviser, Jafco Co., Ltd.

(Slides of MM Morris and Hemmingsen in annex 1)
The "Japan-EU Workshop on Bioventures" was the first opportunity for a direct exchange of experience on biotechnology between Japanese and European business people and scientists. Some mutual knowledge exists in Japan and the EU, however in the field of biotechnology, the general orientation has so far been towards USA. While Japan and Europe have been leading in what may be called "classical" biotechnology i.e. microbiology and fermentation, they both share problems - e.g. rigidity of the university systems – and face several challenges in terms of establishing strong modern biotechnology industry – science-based bioventures. It appears that one of the major obstacles is the historical preference for the big financial/industrial conglomerates and the prestige associated with being employed by them. The workshop demonstrated, however, that ongoing initiatives such as technology transfer organizations and science parks will contribute to the development of a modern biotech industry. As for the change in culture from "big conglomerates-prestige-life-long" to "venture-small-with-growth-potential-change-entrepreneurship", Europe has managed this change at least with some success, and Japan shows signs for doing rapidly so.

The workshop provided an interesting and stimulating introduction to research and business in biotechnology in Japan and Europe. The opportunity to reflect together with European and Japanese policy-makers, business people, financiers and researchers on policy developments, different systems of start-up support and on the different investment climates was a very valuable one. In addition to the discussions in each session of the workshop, the social event - reception after the workshop - offered another, more informal, frame for exchanging information, ask questions and express concerns.

It is important for this exchange of experience which has been set in motion jointly by the Commission and MITI to continue, such as to support the organization of a further event in which these discussions and contacts could be deepened. This event might focus less on strategy issues and more on fostering co-operations in biotechnology between Japanese and European entrepreneurs and scientists, in particular on issues which might enable a more practical and specific interaction between the Japanese and European participants. In developing further the links between the Japanese and European biotechnology holders in research, industry and finance, the following opportunities are highlighted, and could be explored by the EC and MITI:

- Disseminate information in Japan on the third Conference of the European Biotech & Finance Forum, Cambridge, UK, 30Nov & 1Dec. 2000, which focus is on consolidation – new alliances, mergers, partnership between biotech firms.
- Organisation of a special event of the Biotech & Finance Forum dedicated to offering opportunities to showcase bioventures - based in Japan or Europe - and organise one-to-one meetings between Japanese and European prospective partners.
- Organisation of a special Europe-Japan symposium, within the 10th European Congress of Biotechnology - ECB 10 – on 8-12 July 2001 in Madrid, Spain. This symposium could include technical workshop on S&T areas of common interest - e.g. structural genomics -, as well as bioventure presentations.
ANNEXES

ANNEX 1: SLIDES OF SPEAKERS

ANNEX 2: CONTACT DETAILS OF SPEAKERS

ANNEX 3: LIST OF PARTICIPANTS

ANNEX 4: INTERNET WEB SITES