Introducing the New President

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David Smith has worked with the CABI living collection of fungi and bacteria for over 30 years and has been a member of the WFCC for over 20 of those years. Born in the north of England he moved south to Kew to take up a post at the then Commonwealth Mycological Institute on the 24 July 1974. He began work as a freeze-drying and liquid nitrogen storage technologist responsible for the preservation of organisms in the culture collection. Amongst the challenges and varied tasks he integrated the first computer into CMI in 1982 to develop the culture collection database. He worked with Nan Onions, then Curator, benefiting from her vast experience in the management of the world-renowned CMI collection. Together they published their studies on the survival of fungi in preservation and the management of culture collections (e.g. Onions and Smith, 1984; Smith and Onions, 1983a, 1983b, 1994). David became Curator of the renamed International Mycological Institute (IMI) collection in 1987. As part of his research on the preservation of fungi he carried out the first ever cryomicroscopy studies on fungi in 1985 (Coulson *et al.*, 1986). These studies continued and still provide new information on the response of fungi to freezing (Smith and Thomas, 1998; Smith and Ryan, 2004). One of David's proudest moments was the successful completion of his PhD whist working in a full time position at IMI. This would not have been possible without the willing and valuable support of Nan Onions, Colin Booth, Brian Sutton and Dennis Allsopp. In 1989, David was awarded a Japanese Government Fellowship to undertake a study at the National Institute of Agrobiological Resources (NIAR), Japan, where he helped set up protocols for the cryopreservation of *Pyricularia* and *Phytophthora* species. David is particularly proud of his work with Matthew Ryan who is gradually taking over the responsibilities of Curator of the CABI Genetic Resource Collection. Matthew and David have continued the work on improving preservation protocols (Ryan *et al.*, 2001, 2002, 2003). As a part of CABI's mission as a leading global not-for-profit organisation who's purpose is the generation, dissemination and use of knowledge in the applied biosciences to enhance development, human welfare and the environment, David has travelled the world to assist in the establishment of collections, attend and present papers at conferences and take part in training courses. He has visited over 30 countries for example in 1994 he received a Darwin Initiative Award from the UK Department of the Environment to develop a

living collection of microorganisms at LIPI, Bogor, Indonesia. During a recent visit in 2004 to run a training course he discovered that the freeze drier set up during the Darwin project was still operating and the collection was now being supported by a Japanese initiative (1994-1995). He has taught on over 75 training courses in 13 countries with over 1000 participants and has been involved in the training Programs of over 50 individual scientists. He has published more than 90 papers including 70 peer reviewed articles, papers or book chapters and participated in over 46 conferences, presenting over 100 papers and posters in 30 countries. David has particularly enjoyed collaboration in 12 major international projects. He is currently working in CABI member countries, including China, India, Indonesia, Kenya, Malaysia, Tanzania and Uganda to help set up in-country capacity to conserve and utilise microbial diversity.

David has spent many years working with culture collection organisations to help disseminate information and knowledge in the operation and management of culture collections. As a member of the United Kingdom Federation for Culture Collections (UKFCC) he participated in the working group on training courses (1986-1989), was meetings secretary for 1986-1990, was a member of the UKFCC Committee 1997-2000 and has been President of the UKFCC from 1999 to date. Also in the UK he has played a leading role in the establishment of the United Kingdom National Culture Collection (UKNCC) an affiliation of 9 UK national collections (Smith *et al*., 2001). In Europe, David has worked with the European Culture Collection Organisation (Lima and Smith, 2003) and recently resigned his post as President to enable him to carry out the same function for the WFCC. In resigning, he explained that “he had enjoyed his time chairing ECCO, the work with the Executive Board and the members, as President of the WFCC there isn’t the time in the day to do both jobs justice, it was a difficult decision”.

David has moved away from the laboratory bench, although he thinks he can still offer much there. He is fortunate to work with some excellent younger scientists that are more familiar with modern technologies and have better eyesight! He has become more involved with the key issues of long-term sustainability of collections, formulation of common policy, for example in compliance with international conventions, national legislation and regulations, e.g. Biosecurity and international initiatives such as the OECD Biological Resource Centre Initiative (Kelley and Smith, 1997; OECD, 2003; Smith, 2003). He is keen to see culture collections being involved in decision making on issues that impact on their operation rather than merely having to react and change to ensure they meet imposed requirements.

Meeting the WFCC vision

In the three years he will be President, David has committed to help members meet the increasing global demands for worldwide and controlled access to biological resources, public security, industrial quality of their holdings and associated data and the long-term genetic stability of biological material. As President he wishes to facilitate the WFCC to:

    - Provide an effective voice in international initiatives and science policy development
    - Enhance effective electronic communication
    - Support mechanisms to improve the management of preserved biodiversity through common quality and authenticity standards, education and capacity building
    - Develop mechanisms to improve financial resources to support culture collection Programs
- Provide tailored training Programs to meet requirements of international initiatives
- Consolidate and develop the existing international linkages
- Involve national and regional organisations of Culture Collections to enhance collaboration
- Promote the awareness and use of member expertise

He has been a dedicated member of the World Federation for Culture Collections; he was a member of the subcommittee on Postal Regulations, Safety and Quarantine (1988-1992) and chaired this committee from 1992 – 2000 (Smith, 1996). He has been a member of the World Data Center for Microorganisms Steering Group 1998 to 2000 and a member of the Capacity Building and Education Committee (2000-2004). Whist holding the post of secretary (2000-2004) he worked very closely with Jean Swings and contributed to the development of the WFCC strategic plan (see the article in this issue of the Newsletter on the WFCC resolutions from ICCC10 and a perspective of the future). David enjoys life and hopes to bring his enthusiasm and experience to developing the WFCC and supporting its members in their important tasks over the next three years.

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The 10th International Congress for Culture Collections (ICCC-10) (10-15 October, 2004) Tsukuba, Japan

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The 10th International Congress for Culture Collections (ICCC-10) took place at the Tsukuba International Congress Centre (Epochal Tsukuba) in Tsukuba, Japan from 10 to 15 October, 2004, organized jointly by the Japan Society for Culture Collections (JSCC) and the World Federation for Culture Collections (WFCC). The meeting was a legacy for microbiologists of the world of the First International Congress for Culture Collections (ICCC-1) held in Tokyo, Japan in 1968. It was that gathering of 526 participants from 52 countries that had led to the establishment of the World Federation for Culture Collections (WFCC) in 1970 and the holding of the ICCC every four years. Prof. Hiroshi Iizuka, President of ICCC-1, prepared a plaque designed with a ginkgo leaf, signed his name on the reverse side, brought it to ICCC-2 in Sao Paulo in 1973, and suggested that the President of ICCC-2 would sign his name and pass it to presidents of the future ICCCs (cf. Komagata's paper in the proceedings of ICCC-10, 2004). For the 10th Anniversary of the ICCC, the plaque could happily come back to its birthplace. At this historic stage of the ICCC, the meeting brought together a total of 479 participants (including 437 delegates, 18 accompanying persons and 24 guests) from 40 countries and two international organizations, UNESCO and OECD. Among them were more than 180 participants from developing countries and countries with economies in transition. The meeting was sponsored under the framework of UNESCO-Microbial Resources Centres (MIRCENS) Program, the Research Grant of the Institute of Fermentation, Osaka (IFO), Grant-in-Aid for Publication of Scientific Research Results of the Ministry of Education, Culture, Sports, Science and Technology (MEXT), and the Grants of Commemorative Organization for the Japan World Exposition ('70), Tsukuba-City, Suntory Insititute for Bioorganic Research, the Iwatani Naoji Foundation, and the Kao Foundation for Arts and Sciences. The local organizing committee amassed \9,559,580 to support 72 researchers from Russia, Asia, and the Middle and Near East, Africa and South America and \2,392,080 for 23 researchers from developed countries. In addition, under the Symposium Programs of National Institute for Environmental Studies (NIES), the National Institute for Technology Evaluation (NITE), the National Institute of Agrobiological Sciences (NIAS), and the Institute of Chemical and Physical Researches (RIKEN), many promising researchers were invited from developed and developing countries, respectively. This congress could not have been convened without their generous financial support. I am pleased to express our deepest gratitude to all of them.

The congress focused on the important issues in the acquisition, maintenance, provision and utilization of microbial resources. It also benefited from the contributions of numerous fields of scientific specialization

including agricultural, industrial, environmental, health, medical, and the basic sciences. The congress program featured:

1) Prof. Emer. Komagata's plenary lecture, entitled "Milestones in Japanese Culture Collections";
2) Dr. R.A. Samson's pre-banquet lecture, entitled "100 years Centraalbureau voor Schmmelcultures," and Prof. Emer. Komagata's remarks based on the outline of Prof. Colwell's lecture, entitled "Biocomplexity, Global Infectious Diseases, and the Role of Biological Resource Centres" which was cancelled due to unavoidable work commitments.
3) Two special symposia on "Microbial Genomics" (Convener, K. Isono) and "New Paradigms of BRC" (Conveners, J. Swings, M.M. Watanabe & H. Sugawara);
4) Twelve symposia on "Species Concepts of Microorganisms" (Conveners, J. Sugiyama & E. Stackebrandt), "A Quest for Novel Microorganisms" (Conveners, Y. Kamagata & G.M. Garrity), "Extremophiles" (Conveners, M. Kamekura and A. Ventosa), "Fungal Diversity" (Conveners, K. Ando & R.A. Samson), "Algae on Global Environment & Human Welfare" (Conveners, M.M. Watanabe & In Kyu Lee), "Agricultural Microorganisms" (Conveners, H. Kaku & K. O'Donnel), "Probiotics" (Conveners, Y. Benno & Y.K. Lee), "WFCC and International Initiatives" (Conveners, J. Swings & D. Smith), "Regional Role of BRC Network" (Conveners, T. Seki & I. Gandjar), "Human and Animal Cells" (Conveners, Y. Obata & T. Kuwana), "Intellectual Property Rights" (Conveners, P. M. Desmeth & T. Nakahara), and "Biosecurity" (Conveners, T. Ezaki & B. Holmes);
5) Skerman Award Lecture by Dr. Hams-Josef Schroers from Slovenia; and,
6) Eighteen poster sessions, featuring 285 presentations. The following five posters received the Best Poster Award:
   - Brockmann, E., K. Schlichter & C. Sarrazin: Specific detection and quantification of *Bifidobacterium animalis* subsp. *lactis* and *Lactobacillus acidophilis* from different environments by a fluorescent colony hybridization assay.
   - Tanabe, Y. & M.M. Watanabe: The impact of recombination to the genetic diversity of *Microcystis aeruginosa*.
   - Blackburn, S., I. Jameson, C. Johnston, D. Frampton, S. Gallori, M.P. Mansour, P. Nichols, N. Parker, S. Robert, J. Volkman, C. Bolch, A. Negri, L. Llewellyn & M.R. Tredici: The CSIRO Collection of Living Microalgae: An Australian perspective on biodiversity and applications of microalgae.
   - Hongoh, Y., M. Ohkuma, S. Trakulnaleamsai, P. Deevong, T. Inoue, C. Vongkhaluang, N. Noparatnaraporn & T. Kudo: Novel (sub) divisional lineages of bacteria found from the gut of termites.
   - Lestari, Y., C. Andri & A. Tjahjoleksono: The capability of *Streptomyces* sp. PS1-4 in controlling bacterial pathogens on soybean plant in Indonesia.

Prior to the ICCC-10, JSCC organized an open seminar on “Traditional Koji Mold Entering a Modern Gate” convened by T. Okuda and J. Bennett. The seminar had five papers on taxonomy, applications and genome sequencing of the Koji mold (*Aspergillus oryzae*) and the life and work of Dr. Jokichi Takamine who was the first to apply the enzymatic activity of *A. oryzae* to modern industry. Especially the paper regarding Dr. J. Takamine reminded us of his contribution to early biotechnology but also to cultural understanding on the 150th anniversary of his birth.

The proceedings of the ICCC-10, “Innovative Roles of Biological Resource Centres,” edited by M.M. Watanabe, K. Suzuki and T. Seki were published before the meeting and presented to each participant upon registration. The proceedings are composed of three parts. Part I includes 16 chapters and 78 full papers from plenary lectures, the open seminar, two special symposia and 12 general symposia. Part II provides two special lectures. Part III includes 312 abstracts submitted for the poster presentations. All the full papers of Part I were peer-reviewed by the conveners of each session. The proceedings could simultaneously provide the participants with the most up-to-date information on innovative roles of biological resource centres and lead every participant to a deeper understanding of the microbial works of others and a lively exchange of their ideas. I am happy to express my deepest gratitude to many scientists who convened the open seminar, plenary lectures, special symposia, and general symposia and who served as peer-reviewers for the manuscripts submitted for the proceedings.

Preparing this ICCC-10 was a full four-year task. I initially presented the Japan candidacy. We in Japan were happy that our country was chosen to host this congress on the 10th anniversary of the ICCC. The local organizing committee (chair: M.M. Watanabe) was convened in 2001, the same year as the program committee (chair: T. Seki) and the fund-raising committee (chair: Y. Benno). I am pleased to thank all of the members of these committees most sincerely, and especially Prof. Emer. K. Komagata, adviser of the local organizing committee, Prof. K. Nishimura, President of JSCC and Dr. K. Suzuki, vice-chairs of the local organizing committee and program committee, who contributed actively to congress preparations.

I would also like to thank the staff of the congress secretariat: Dr. F. Kasai, Dr. M. Hiroki, Dr. M. Kawachi, Dr. M.H. Noel, Dr. Y. Oomura, Dr. Y. Tanabe, Dr. S. Hirabayashi, Dr. H. Itayama, Mr. A. Higa, Ms. T. Kotani, Mrs. K. Takei, Ms. T. Kato, Mrs. K. Yamamoto, Dr. M. Erata, Ms. F. Mori, Mr. K. Yumoto, Dr. M. Moriya and Ms. M. Ishimoto, Biological Resource Collections at the National Institute for Environmental Studies, who, through their friendliness and efficiency, greatly contributed to preparing the congress and warmly welcomed the participants. I would like to express special thanks to Dr. F. Kasai for her dedicated work in organizing the congress.

And lastly, I thank all the participants of the ICCC-10. The quality of your scientific contributions made this congress a great one. I hope your stay in Tsukuba was as enjoyable and fruitful as we had wished it to be. I hope that

you took home good memories of enjoyable and friendly encounters as well as a scientifically enriching exchange.

Milestone in Japanese Culture Collections

by Prof. Kazuo Komagata
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Japanese universities, national institutes, private sectors have been interested in culture collections related to traditional fermentations and modern microbial industry. Japanese culture collections have mainly grown in response to the social needs to solve problems in the traditional fermentation and to develop modern microbial processes. The establishment of the first service culture collection in Japan dates back to 1904. After World War II, the Japan Federation of Culture Collections of Microorganisms (JFCC) (now Japan Society for Culture Collections, JSCC) was organized in 1951 for encouraging research on microorganisms and exchanging microbial information by the recommendation of the Ministry of Education, the Government of Japan. The JFCC organized the First International Conference on Culture Collections (ICCC-1), and contributed to the establishment of the World Federation for Culture Collections (WFCC). The JFCC-JSCC has since been working for strengthening Japanese culture collections and international cooperation with overseas culture collections. The JSCC aims to renew the Japanese culture collections to modern biological resource centers with the highest standard, and to expand microbial networks in cooperation with other collections throughout the world. Further, the building of a “human network” is essential for the further development of the culture collections.

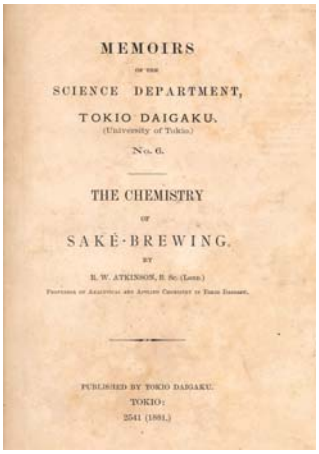
Introduction

Japanese culture collections have mainly grown in response to the social needs to solve problems in traditional fermentations and to develop modern microbial processes. The Japanese traditional fermentation is recorded about 1,000 years ago. Since 17th century, conidia of *Aspergillus oryzae* grown on steamed rice have been collected and used for koji starters (*tane koji*). Koji is steamed rice grown with *A. oryzae* inoculated with the koji starter, and is widely used for making saké, soy sauce, soy bean paste (*miso*), and other fermented products. Thus the koji starter is important for the Japanese traditional fermentation. It is recorded that feudal lords strictly regulated the production of the koji starter and collected tax from its sale (Sakaguchi, 1964). Koji molds, yeasts, and lactic acid bacteria have been employed for the Japanese traditional fermentation. Saké is a national drink. Shochu is a spirit made from rice, sweet potato, and other starchy materials and is popular as well. Soy sauce and soy bean paste are fermented products of soy beans and are still important seasonings for the Japanese. Recently, soy sauce has become used worldwide. Vinegar was traditionally produced from saké and saké cake by surface culture, but now it has been produced by submerged culture.

Teaching and Research on Applied Microbiology in Japan

In 1877, the Komaba Agricultural College (now the Faculty of Agriculture), the University of Tokyo was established. Teaching of applied microbiology started

and intensive research in taxonomy, biochemistry, and physiology of microorganisms involved in the Japanese traditional fermentation has been carried out. Modern research of applied microbiology was introduced by teachers invited from overseas countries about 130 years ago. An English chemist, Prof. Atkinson, R. W. studied the saké making, and published “The Chemistry of Saké Brewing” in 1881 (Fig.1) (Atkinson, 1881). This study deals with koji, referring to rice (raw material), preparation of koji, action of koji extract upon cane sugar, maltose, and dextrin, and action of koji upon gelatinized starch. Further, he mentioned the saké making, dealing with preparation of starters (*moto*), the principal of process, fermentation of the mash, filtration of saké and yield of alcohol, preservation of saké, and shochu and mirin (sweetened saké). He included an illustration of the saké-brewery in 1789 (Fig. 2). This study is the first scientific monograph of the saké making in English.


MEMOIRS

OF THE

SCIENCE DEPARTMENT,

TOKIO DAIGAKU.

(University of Tokio.)

No. 6.

THE CHEMISTRY

OF

SAKÈ-BREWING.

BY

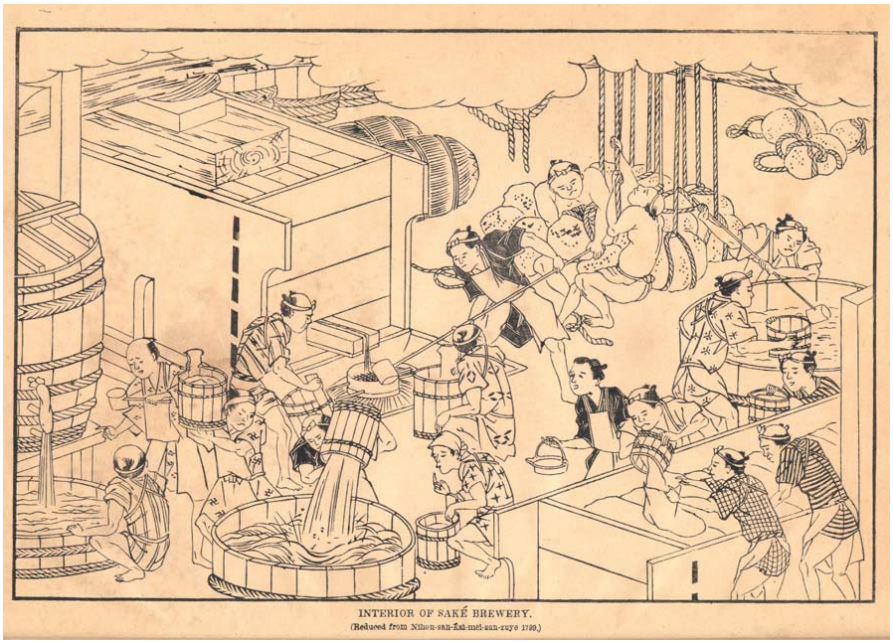
R. W. ATKINSON, B. Sc. (Lond.)

PUBLISHED BY TOKIO DAIGAKU.

TOKIO:

2541 (1881.)

Fig. 1. Atkinson, R. W.: The Chemistry of Saké Brewing (1881).


INTERIOR OF SAKÉ BREWERY.

(Reduced from Nihon-san-Zai-mei-san-zuye 1789.)

Fig. 2. Atkinson, R. W.: Saké brewery in 1789 (1881)

Agricultural colleges have been established in other universities since the opening of the Komaba Agricultural College, and teaching and research on applied microbiology have been extended in Japan.

Culture Collections in Japan before World War II

Japanese universities, national institutes, and private sectors have been interested in culture collections related to the traditional fermentation and modern microbial industry. Lineage of the Japanese culture collections is depicted (Fig. 3) (Hasegawa, 1996b).

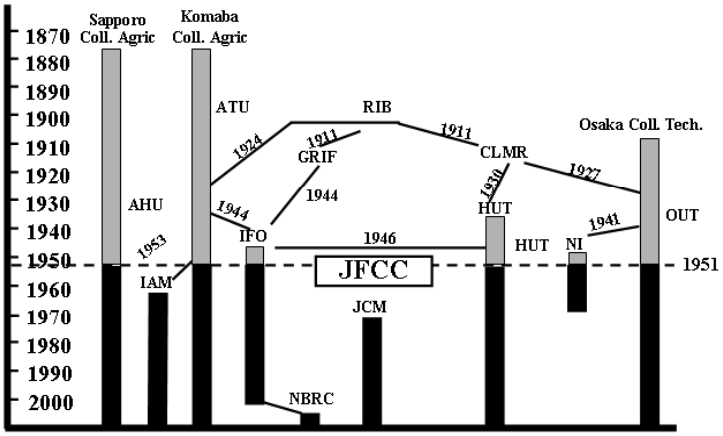


Fig. 3. Lineage of Japanese Culture Collections.

(Modified Hasegawa's original. Abbreviations: AHU, Faculty of Agriculture, Hokkaido University; ATU, Faculty of Agriculture, The University of Tokyo; CLMR, Central Laboratory, South Manchuria Railway Co., Ltd. (defunct); GRIF, Government Research Institute, Formosa (defunct); HUT, Faculty of Engineering, Hiroshima University; IAM, Institute of Applied Microbiology, (now Institute of Molecular and Cellular Biosciences), The University of Tokyo; IFO, Institute for Fermentation, Osaka (defunct); NBRC, NITE Biological Resource Center; NI, Nagao Institute (defunct); OUT, Department of Fermentation Technology (now Department of Biotechnology). Osaka University; RIB, National Institute of Brewing).

The first Japanese service culture collection to be established dates back to 1904. The Tax Administration Agency of the Government of Japan undertook basic and applied studies of making saké and other fermented products, and set up the Brewing Experimental Station (now National Institute of Brewing). A culture collection of microorganisms was located at the Station (RIB) charged with the distribution of microbial cultures on demand (Hasegawa, 1996a). Another early and noteworthy culture collection was the Central Laboratory of the South Manchuria Railway Company (CLMR) at Dairen, Manchuria, (now Dalian, Liaoning Province, China) (Hasegawa, 1996a). These culture collections were major sources of microbial cultures before World War II, but

the culture collections were damaged during the war. Part of the RIB collection has been maintained at the Laboratory of Fermentation, the University of Tokyo, and its holding was then distributed to the Culture Collection of Institute of Applied Microbiology (IAM) (now Institute of Molecular and Cellular Biosciences), the University of Tokyo. Part of the CLMR collection was moved to Hiroshima University and Osaka University (Hasegawa, 1996a). While, the Government Research Institute, Formosa (GRIF) (Taiwan) contributed to the development of Japanese culture collections. Microorganisms involved in indigenous fermented products in Taiwan and utilization of molasses were studied, and systematic studies of *Rhizopus*, *Monascus*, *Aspergillus* and other microorganisms were extensively studied. Part of the microorganisms was distributed to Takeda Pharmaceutical Company in 1939, and following years, the microbial cultures became a core collection of Institute for Fermentation, Osaka (IFO), and they were further distributed to other Japanese culture collections (Hasegawa, 1996a).

The very first service culture collection in the world is reported to be the Král Culture Collection founded by Dr. František Král in Prague probably in 1890 (Kocur, 1990; Porter, 1976). Thus the RIB was established at a similar time to the Král collection.

Nagao Institute (NI) was established in 1941, and published a catalogue of microbial cultures in 1950. This institute was a leading culture collection in Japan but was defunct in 1971 (Hasegawa, 1996b). Institute for Fermentation, Osaka (IFO) was established in 1945 (Hasegawa, 1966b). IFO was one of the most active culture collections in the world, and distributed large numbers of microbial cultures worldwide. However, its holding was transferred in 2002 to the Biological Resource Center (NBRC), the National Institute of Technology and Evaluation.

Culture Collections in Japan after World War II

The Higher Education and Science Bureau of the Ministry of Education, the Government of Japan carried out a survey in 1952 on microbial cultures preserved in research organizations, including universities, national institutes, and private sectors. It concluded that 22,300 cultures were maintained in 251 culture collections belonging to 144 organizations. The Bureau published *A Catalogue of Cultures of Microorganisms Maintained in the Japanese Culture Collections* in 1953 (Fig. 4) (The Higher Education and Science Bureau of the Ministry of Education, the Government of Japan).

The catalogue was edited by Dr. K. Kominami and scientific names of holdings, the history of the cultures, and culture collections preserving the cultures were described. The publication of the catalogue brought a deep interest in microbial cultures to Japanese microbiologists, and resulted in raising a project of reidentification of microbial cultures maintained in Japanese culture collections. The project continued 11 years and about 100 researchers were involved in it. Reidentified cultures were deposited to Japanese culture collections, and the collections were enriched their holdings in consequence.

Fig. 4. General Catalogue of the Cultures of Microorganisms Maintained in the Japanese Culture Collections (1953).

After World War II, penicillin production was introduced from USA and quickly and successfully developed and industrialized. Research has since been pursued new antibiotics energetically. Large numbers of useful strains have been isolated from natural sources and mutants with high potential have been screened. IFO and other Japanese culture collections supplied microbial cultures to researchers on demand. Consequently, large numbers of new antibiotics were found by Japanese workers, and have appeared on the market. In 1946, the Japan Penicillin Research Association, (now the Japan Antibiotics Research Association) was established for the promotion of the research and industrialization of antibiotics. Its members were from universities, national institutes, and private sectors, and they made their data open and public. The association contributed to the substantial development of research and the production of antibiotics in Japan. This type of the organization is a forerunner model for cooperation of workers involved in research of microorganisms. The organized cooperation led to success in research and industrialization of glutamic acid and other amino acids, and nucleosides and nucleotides.

Japanese Federation of Culture Collections of Microorganisms (JFCC)

The Japanese Federation of Culture Collections of Microorganisms (JFCC) was founded in 1951 following the recommendation of the Ministry of Education, the Government of Japan and Science Council of Japan (Hasegawa, 1996b). The aim of the federation is to encourage research on microorganisms and to exchange information on microbial cultures. The federation encompassed the Japanese culture collections in the fields of general microbiology, medical microbiology, applied microbiology, and environmental microbiology, and consisted of only 11 culture collections at the start. The JFCC was the first network of culture collections and data bank in Japan (Komagata, 1977). In response to social needs and growth of microbiology, the federation changed the name to the Japan Federation for

Culture Collections (JFCC), and any culture collections in Japan and persons who are interested in culture collections and microbiology became enrolled as members of the JFCC. Further, the JFCC changed the name to the Japan Society for Culture Collections (JSCC) in 1993. In commemoration of the development and progress of the Japan Federation of Culture Collections of Microorganisms, the JSCC organized and held the 50th anniversary, and commemorative lectures were presented in 2001 (Komagata, 2001a, b).

The First International Conference on Culture Collections (ICCC-1)

The delegation of the Government of Japan submitted a proposal to 12th General Conference of UNESCO in 1962 as recommended by the JFCC (Hasegawa, 1996b; Komagata, 2001b). It included the followings: (1) the development of culture collections on a worldwide scale; (2) the development of research on microorganisms; and (3) the training of researchers in both of the fields. The proposal was adopted at the 13th General Meeting of UNESCO in 1964 as a long-term project entitled “Promotion of Research of Microorganisms”. Consequently, UNESCO held the International Meeting of Specialists on Microorganisms in Paris in 1966, and representatives of UNESCO, the Section of Culture Collections of International Association of Microbiological Societies (IAMS) (now the International Union of Microbiological Societies, IUMS), the JFCC, WHO, and FAO discussed plans of the long-term project. The meeting made the following recommendations to the Section on Culture Collections of IAMS: (1) a worldwide survey of culture collections; (2) the preparation of a world directory of culture collections; (3) the training of researchers; (4) the promotion of exchange of cultures; (5) standardization of terminology, methods of determination and recording of research information; (6) the convention of international conference; and (7) the organization of an international federation. These recommendations were considered by the Section of Culture Collections of IAMS, and were approved by the Executive Committee of IAMS and the ICRO-UNESCO Panel on Microbiology. Japan was requested to hold an international conference as the original proposer of the project. The JFCC discussed the matter with the Japanese National Council of Science and the Japanese Commission for UNESCO, and organized the conference in Japan. Thus the First International Conference on Culture Collections (ICCC-1) was held in Tokyo in 1968 (Iizuka and Hasegawa, 1970; Hasegawa, 1966b; Komagata, 2001a). The JFCC played important roles in the holding of ICCC-1, and 526 persons from 52 countries participated in the conference. Resolutions were unanimously decided and consisted of 7 items. They are (1) the recommendation of International Federation of Culture Collections; (2) the holding of conference of culture collections; (3) investigation on the need for special training course; (4) the establishment of reference laboratories; (5) the establishment of international centers for characterization of strains of microorganisms; (6) the provision of laboratory supplies and cultures to development countries; and (7) a feasibility study on the establishment of an international center for information (Iizuka and Hasegawa, 1970). This can be regarded as the first guideline of the World Federation for Culture Collections.

Prof. Iizuka, President of ICCC-1 prepared a plaque designed with a ginko leaf, which was regarded as the symbol of the ICCC. The plaque was made of a piece of 800-year-old wood of ebony (*Diospyros ebenum*). Ginko leaves mean “expanding horizons” for the Japanese people (Iizuka, 1977). He brought the plaque to ICCC-2 in Sao Paul in 1973, and suggested that President of ICCC-2 would sign his name on the reverse side and pass it to Presidents of the future ICCCs (Iizuka, 1973; Iizuka, 1977). After a long journey, the plaque has happily returned back to Japan. This tells us of sincere endeavor and cooperation of culture collection people in the world who contributed to the development and improvement of the culture collections.

World Federation for Culture Collections (WFCC)

Importance of culture collections was recognized about 70 years ago. The First International Congress of Microbiology was held in Paris in 1930, and a Commission of Nomenclature and Taxonomy was constituted to report recommendations to the Plenary Session of the Congress (Editorial Board for Bacteriological Code, 1992). According to recommendations made by several of the delegates to the congress, a commission mentioned the significance of culture collections as follows: “Among the most important agencies working toward satisfactory nomenclature and classification of bacteria are the several type culture collections. These constitute invaluable repositories and much of the future development will depend upon their adequate growth, support and utilization; in some cases at least they should develop to research institutes of high grade. ·It is further urged that all bacteriologists publishing descriptions of new species or important strains of bacteria deposit pure cultures of such with a culture collection that may be made available to others interested”. However, implementation of the resolution was not progressed as would be expected.

The cooperative program of culture collections was recognized in some countries. International Federation of Culture Collections (IFCC) was set up in 1947 on the occasion of the 4th International Congress of Microbiology, and its office was located at Centre de Collections de Types Microbiens at Lausanne in Switzerland. However, the IFCC was defunct in 1954 (Hasegawa, 1996b). The British Commonwealth Scientific Official Conference (BCSOC) was held in UK in 1946. The Specialists Congress of Culture Collections of Microorganisms was held in London in 1948, and the United Kingdom National Committee of the British Commonwealth Culture Collection was organized (Cowan, 1950; Gibbons, 1963). Following the committee, the Permanent Committee of the British Commonwealth Collection of Microorganisms was set up in 1948. Further, the Canadian Committee on Culture Collections was established in 1948 because the BCSOC expected the establishment of an international cooperative organization of culture collections. Consequently, the Specialist’s Conference on Culture Collections was held in Montreal in 1962, and its main issue was “Culture Collections: Perspective and Problems” (Martin, 1963). IAMS adopted the resolution of the conference, and the Section on Culture Collections was organized in 1963.

The Executive Board of IAMS prepared plans with the constitution and rules of the section in 1964 (Hasegawa, 1996b; Komagata, 2001a).

The resolution of ICCC-1 recommended the establishment of International Federation of Culture Collections. The meeting of the Section on Culture Collections in IAMS was held on the occasion of the 10th International Congress of Microbiology in Mexico City in 1970, and the future plans of an international organization were discussed. Thus the Section on Culture Collections in IAMS was dissolved, and the World Federation for Culture Collections (WFCC) was constituted (International Association of Microbiological Society, 1972a, b; Porter, 1976). Officers were then Dr. Martin, S. (Canada), President; Dr. Iizuka, H. (Japan), Vice-president: Dr. Lapage, S. (UK), Secretary; Skerman, V. (Australia), Tresurere; Hoffmann, S. (Germany); Lesesel, E. (USA); Papavassiliou, J. (Greece); and Piéchaud, M. (France).

Thus the WFCC came to be established based on national and international considerations for a cooperative network of culture collections. The JFCC took part in the establishment of the WFCC as well.

The World Data Center (WDC) (now the World Data Center for Microorganisms, WDCM) was relocated from the Queensland University in Australia to the Institute of Physical and Chemical Research (RIKEN) in Japan in 1986 (Komagata, 1987), and then moved to the National Institute of Genetics in 1996 (Sugawara, 1998).

The Activity of the Japan Society for Culture Collections (JSCC)

The JSCC holds a general meeting once a year to discuss the activity of the member collections and considers international trends in culture collections. A total of 25 culture collections are affiliated with the JSCC in 2004. The JSCC member collections hold a total of 229,840 cultures in 2003 (Report of Japan Society for Culture Collections, 2004). Of the cultures, 44,188 are filamentous fungi (19.2%), 25,319 yeasts (11.0%), 8,319 actinomycetes (3.6%), 145,285 bacteria (63.2%), 638 viruses (0.3%), 2,015 microalgae (0.9%), and 4,022 others (1.7%). The JSCC member collections distributed 22,544 cultures to domestic and overseas researchers and organizations in 2003 (Fig. 5).

The journal of *Microbiology and Culture Collections* is published twice a year by the JSCC, containing original papers covering the systematic study of microorganism, development of microbial preservation, and other related studies. Further, the JSCC awards the two JSCC Prizes to persons who contributed to the development of preservation of microbial cultures and the systematic study on microorganism. Thus the JFCC-JSCC has paid attention to maintenance of a variety of cultivable microorganisms, and encouraged the Japanese culture collections and persons who are interested in culture collections and microbial systematics. On these circumstances, the Japan Collection of Microorganisms (JCM) was established in 1980, and Biological Resource Center (NBRC), National Institute of Technology and Evaluation was set up in 2002. Thus the activity of the JSCC has been strengthened.

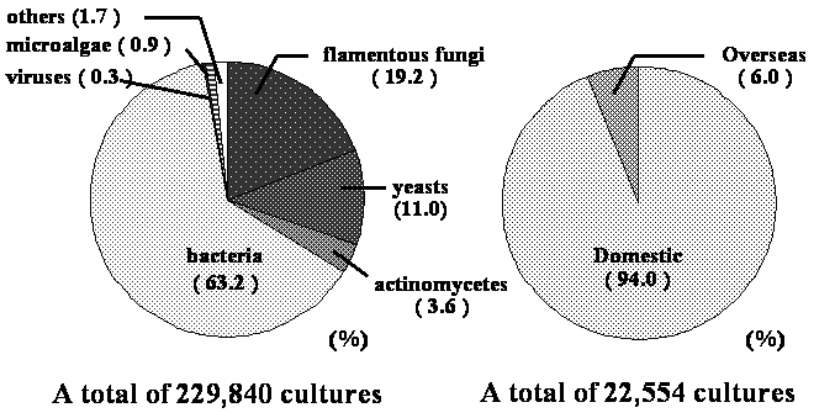


Fig. 5. The Activity of Japan Society for Culture Collections (JSCC).

Left: Holdings of the member collections of JSCC. Right: Distribution of cultures by member collections of JSCC.

The Japanese prominent bacteriologists, Dr. Kitasato, S., Dr. Shiga, Y. and other microbiologists have been working in the field of medical microbiology, but culture collections on medically important microorganisms had been private collections or laboratory scaled collections. Recently, Research Center of Emerging Infectious Diseases (RIMD), Osaka University; Research Center for Pathogenic Fungi and Microbial Toxicoses (IFM), Chiba University; Institute of Medical Mycology (TIMM), Teikyo University; Department of Microbiology (GTC), Gifu University School of Medicine and other specialized collections are core collections in the JSCC.

Genebank, National Institute of Agrobiological Sciences (MAFF) is a specialized collection for plant pathogens and other microorganisms related to agricultural sciences. The Microbial Culture Collection at the National Institute for Environmental Studies (NIES) is an algal collection to support environmental research.

Both the International Patent Organism Depositary (IPOD) at the National Institute of Advanced Industrial Science and Technology and the NITE Patent Microorganisms Depository (NITE NPOD) at National Institute of Technology and Evaluation have played a role in the international depository of patent organisms.

Retrospective and Perspective

Since the early days of microbiology, astronomical numbers of microbial strains have been isolated from a wide variety of natural sources and used for scientific research and microbial industry. However, large numbers of microbial cultures had lost in the past, and they are no longer available. Microbiologists often lose the microbial cultures that they studied because of the change of their interests and difficulties in keeping the cultures. This negative outcome is due to the absence of reliable culture collections in which the microbial cultures can be maintained properly and supplied promptly on demand.

Through the study of microbial cultures maintained in culture collections, potential properties of microorganisms have been developed and the future perspective of microbiology can be foreseen. Effective research needs adequate and reliable sources of properly preserved cultures. In the near future, very large numbers of microbial cultures will be isolated through the study of biodiversity, and the attributes of large numbers of the cultures will be improved. Therefore, reliable and well-organized culture collections are needed as depositories and for the promotion of research and application of the cultures. In fact, culture collections play a key role in maintaining the type strains in bacteriology, and the study of bacterial systematics cannot be completed without reliable culture collections in consequence.

Microorganisms are widely used for biological studies and new advances in biochemistry, genetics, and molecular biology are essentially due to the study of microorganisms as a model of life. Microorganisms are not only of value for the production of useful substances, but they also play unique roles in element cycles with plants and animals. To a great degree, humans depend on individual microorganism in biotechnology and diverse ecosystems on the earth. Microorganisms are also significant gene pools, and these gene pools must not be lost. From this point of view, microorganisms can be regarded as a cultural heritage and cultural property, and must be transferred to the next generation in a normal and healthy condition.

Needs of society for culture collections are increasing year-by-year and their effective and smooth management is required. Exchange of information and cooperation among culture collections are crucial. Enhancement of culture collections is a key element for the future development of microbiology, microbial industry, and biotechnology. In addition, the good operation and management of culture collections are in great part due to the activity of highly trained and experienced personnel working in the culture collections.

The JFCC-JSCC has been working for strengthening Japanese culture collections and international cooperation with overseas culture collections. Further, the JFCC organized the ICCC-1, and contributed to the establishment of the WFCC. The JSCC aims to renew the Japanese culture collections to modern biological resource centers with the highest standard, and to expand microbial networks in cooperation with other collections

throughout the world. Further, the building of a “human network” is essential for the further development of the culture collections.

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WFCC Patent & Industrial Property Committee
Summary report of activities 2000 – 2004

by Dr. Philippe Desmeth

Introduction

The activities of the WFCC Patent & Industrial Property Committee have been focused on the developments in the matter of intellectual property rights (IPR) related to genetic resources, considering its impact on the operations of culture collections in the world. IPR related to genetic resources have been top issues in two main fora.

The "*Intergovernmental Committee on Intellectual Property and Genetic Resources, Traditional Knowledge and Folklore*" (IGC), established under the auspices of the World Intellectual Property Organization (WIPO), has concentrated on examining the relationship between intellectual property and genetic resources in the areas of contractual agreements for access to genetic resources, legislative, administrative and policy measures to regulate access to genetic resources, and the protection of biotechnological inventions.

The CBD working groups and assemblies are working to set up international rules to implement the principles of ABS stated in articles 1, 15 and related.

Follow up and lobbying in international bodies

WFCC has the status of permanent observer at the World Intellectual Property Organization (WIPO), in recognition for its work in the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure. This treaty is a corner stone in the implementation of the patent system in biotechnology inventions involving microbiological resources.

In WIPO, the Committee chair represented WFCC during most of the 6 sessions of the "*Intergovernmental Committee on Intellectual Property and Genetic Resources, Traditional Knowledge and Folklore*" (IGC), which all took place in Geneva (April 30 to May 3, 2001; December 10 to 14, 2001; June 13 to 21, 2002; December 9 to 17, 2002; July 7 to 15, 2003; March, 15 to 19, 2004). The IGC deals with intellectual property related to genetic resources, a matter that lay at the crossroads of the Convention on Biological Diversity (CBD) and the Trade-Related Aspects of Intellectual Property Rights (TRIPS). The orientation or the decisions taken by the IGC can affect operations of biological resources centers such as culture collections. The IGC has already acknowledged the work done by WFCC members in a document [1] prepared for the purpose of the second session. We can also underline that the status of permanent observer of WFCC has been revitalized during this period.

Since ABS issues tackled in the CBD "*Ad Hoc Open-Ended Working Group on ABS*" have an impact on IPR and propose IPR as one way to organize benefit-sharing, the Committee is also following the ABS issues in the various

competent forum of the CBD. In the CBD arena, the Committee has been pleading for applicable solutions and alternatives based on technical facts, practical constraints and scientific evidence instead of counterproductive or inapplicable rules resulting from political negotiations and arrangements where practical considerations are often badly overlooked.

Members of the Committee have been actively involved in CBD meetings as individual experts, as official representatives of their respective countries or much better as WFCC representatives. The position of WFCC in this matter is that the "*Bonn guidelines on access to genetic resources and the fair and equitable sharing of the benefits arising from their utilization*" [2] are a good framework to design appropriate branch / sectorial implementation such as the MOSAICC [3] initiative. WFCC participation to the CBD ABS forum is acknowledged in several CBD documents [4].

Key CBD meetings attended by WFCC members included the first meeting of the Ad Hoc Open-ended Working Group on Access and Benefit-Sharing in Bonn, Germany (22 to 26 October 2001), the Open-ended expert workshop on capacity-building for access to genetic resources and benefit-sharing (2 to 5 December 2002 - Montreal, Canada), and the second meeting of the Ad Hoc Open-ended Working Group on Access and Benefit-Sharing (1 to 5 December 2003 - Montreal, Canada).

Participation to international venues

Providing information and training on IPR related to genetic resources to WFCC members is important because the role of culture collections is not limited to providing microbiological material and services. Answering the needs of customers, culture collections are increasingly becoming consultants and brokers in legal administrative matters such as IPR, import-export modalities and other commercial transactions.

The Committee has not yet published a handbook on IPR related to microbial genetic resources but it hopes to open a website soon dedicated to this topic. Nevertheless, to disseminate information about IPR and to make culture collections aware of their impact in their daily operations, the Committee has organized, facilitated or participated to several international venues.

It has organized, in coordination with WIPO, the Workshop on "Intellectual Property Rights related to Microbial Genetic Resources". A one-day workshop on intellectual property rights (IPR) related to microbial genetic resources (MGR) as a satellite meeting to the IX International Congress of Culture Collections (Melbourne, 28 July 2000).

It has induced the organization of a Conference on the Budapest Treaty and the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure. This conference was organized in Casablanca, Morocco, on 16 and 17 April 2002, by WIPO' Arab office and Patent Law office, the Moroccan National Center for Scientific and Technical

Research and the Moroccan Organization for Industrial and Commercial Property.

The Committee chairman has participated to the «International Symposium on Microbial Resources» at the Yunnan University, Kunming, PR.China. (6 to 9 August 2002) to present the role of Intellectual Property Rights to support biotechnology developments and industrial use of microbial resources.

The Committee is also actively involved in the issue of property rights related to biodiversity data as well as data and database protection. This topic is becoming increasingly important because the information related to microbiological resources are as important as the resources themselves.

The Committee presented this issue during the workshop entitled “Towards a global infrastructure for microbial information” jointly organized by WFCC, the Global Biodiversity Information Facility (GBIF) and the Belgian Coordinated Collections of Micro-organisms (Brussels, 27 – 28 October 2003).

The Committee chair has also participated to the GBIF Experts’ Meeting on biodiversity data, databases and property rights issues. (Royal Botanic Garden, Madrid, Spain, 1-2 March 2004). The purpose of this meeting was to design the rules applicable to providers and users of data accessed via the GBIF portal.

The participation of the Committee chair to the WFCC workshop on “Commercial Use of Microbial Diversity” during the 13th International Symposium on the Biology of Actinomycetes (Melbourne, 1 to 8 December 2003) was an opportunity to enlarge the dialogue with companies and public authorities on the financial and administrative management of culture collections.

The Committee also participated in the WFCC-USFCC-BCCM-CCMM/CNRST [5]. Training course on Management of Culture Collections of Microorganisms (Rabat, 3-7 May 2004). We believe that such training is most useful when culture collections have to evolve from traditional depository facilities to biological resource centers which supposes that management is also evolving. Indeed, managing activities are broadening from pure scientific and technical management of microbial assets to businesslike management including control of the operational legal, regulative and commercial aspects. This move is necessary for a culture collection to survive in a competitive environment and to participate in global science.

Involvement in international projects

To revitalize the work initiated during the WFCC workshop on Economic Value to Microbial Genetic Resources (12 August 1998, Halifax, Canada), the Committee chair has initiated and leads the project MOSAICS [6] which seeks the development of an integrated system to manage the Access and Benefit Sharing (ABS) issues related to microbial resources. This project is funded by the Directorate General Research of the European Commission. It has three

operational objectives, including the development of adapted or new reliable ways to value microbial resources. The Committee chair secured the participation of WFCC and of five culture collections from different continents.

In short, during the period 2000-2004.

- The WFCC Patent and Industrial Property Committee contributes to revitalize the WFCC status of **permanent observer at the World Intellectual Property Organization** (WIPO), by actively participating to the "***Intergovernmental Committee on Intellectual Property and Genetic Resources, Traditional Knowledge and Folklore***".
- The committee is following the **Access and Benefit-Sharing** (ABS) issue in the various competent fora of the **Convention on Biological Diversity** because ABS has an impact on IPR. It is pleading for applicable solutions designed by professionals for professional microbiologists.
- The committee is **organizing informative and work sessions on IPR related to microbial resources** when financial support is possible, in the context of international scientific venues or during training courses.
- The committee is also involved in the issue of property rights related to biodiversity data, including **data and database protection**, notably in the framework of the **Global Biodiversity Information Facility.**

References

1] "Operational principals for intellectual property clauses of contractual agreements concerning access to genetic resources and benefit-sharing". WIPO/GRTKF/IC/2/3; September 10, 2001.

2] The *Bonn Guidelines* were defined during the Ad Hoc Open-ended Working Group on Access and Benefit-Sharing in Bonn, Germany, from 22 to 26 October 2001. They were adopted at the sixth meeting of the Conference of the Parties.

3] MOSAICC stands for "*Micro-Organisms Sustainable use and Access regulation International Code of Conduc* ". The aim of the project was to design a tool for microbiologists to implement the CBD at the microbial level, in accordance with other relevant rules of international and national laws. It was funded by the European Commission (Directorate General Research). MOSAICC was issued in spring '99, following a workshop where about 40 experts of 15 different nationalities were invited to comment and amend the proposal. The MOSAICC Code of Conduct now available on internet (http://www.belspo.be/bccm/mosaicc) is the result of five successive drafts improved through dialogue between MOSAICC partners (including WFCC and

WFCC members) and other experts. Although written two years earlier, MOSAICC is fully compatible with the Bonn guidelines.

4] Review of options for access and benefit-sharing mechanisms (II. D. 2. 36.) (UNEP/CBD/ISOC/3; 11 March 1999). CBD Intersessional meeting on the operations of the Convention (ISOC, Montreal, 28-30 June '99). This document mentions the WFCC document on "Access to Genetic Resources within the Framework of the CBD" and the MOSAICC project funded by the European Union.

- Report of the Panel of experts on Access and Benefit-Sharing on the work of its first meeting. Contents D. The concept and procedure of prior informed consent .p.6 and paragraph 124 p.30 (UNEP/CBD/COP/5/8; 2 November 1999)
- COP-5 conclusions V/26 A. 6. «[The COP] Notes that, voluntary measures, including guidelines, may help ensure realization of the objectives of the Convention, and to that end invites the parties to consider promotion of their use.» (UNEP/CBD/COP5/23 & 23/ANX3; 22 June 2000)
- CBD Ad Hoc Open-Ended working Group on Access and Benefit-Sharing (First meeting, Bonn, 22-26 October) Development of draft international guidelines on access and benefit-sharing - Elements for consideration in the development of guidelines and other approaches for access to genetic resources and benefit-sharing (UNEP/CBD/WG-ABS/1/3; 11 August 2001).

5] USFCC : US Federation for Culture Collections
BCCM: Belgian Coordinated Collections of Micro-organisms
CCMM: Moroccan Coordinated Collections of Micro-organisms
CNRST : Moroccan National Center for Scientific and Technical Research

6] Micro-organisms Sustainable use and Access management International Conveyance System (see http://www.belspo.be/bccm)

WFCC Committee on Postal, Quarantine and Safety Regulations Report 2000-2004

by Dr Christine Rohde

The detailed report by the PQSR Committee representing its activities, developments and concerns is available online at http://www.wfcc.info/index.html

The report is also freely available as printed brochure. Please, direct your order to Dr. Christine Rohde, DSMZ (chr@dsmz.de).

Through the last period of office, this committee had eleven members. Several main issues of the work plan turned out to be milestones for this committee and for the scientific community. A summary is given below:

Summary on the work of the WFCC PQSR Committee

The WFCC Postal, Quarantine and Safety Regulations (PQSR) Committee looks back to almost 30 years of existence: WFCC Newsletter No. 1, March 1975, announced the establishment of a Committee on Postal and Quarantine Regulations having the aim to collect and disseminate information on the relevant regulations. This demonstrates that even in the *pre* gene technology era, at times when bioterrorism was not a catchword, when dangerous goods shipping questions were not dominating daily life in the shipping departments of the Culture Collections and when biosafety and biosecurity did not receive as much attention as nowadays there was a demand to have a group among WFCC looking closer at the regulations. Scientists had to become familiar with all the regulations governing handling and distributing of biological materials. Over the years, the name of this Committee slightly changed, the list of the Committee members grew and so did the list of aims and goals. As for other WFCC Committees, it is of high relevance to have enough members who are working at Culture Collections/Biological Resource Centres in different regions all over the world. Actually, the PQSR Committee has twelve members in eleven countries. During the last term of office the achievement of some milestones needed a lot of attention. The most outstanding one was receiving observer status to the United Nations Sub-Committee of Experts on the Transport of Dangerous Goods (UNSCETDG) and the succeeding negotiations on shipping deregulations for Risk Group 2 cultures. The expectations regarding the latter had been very high.

The bioterroristic anthrax attacks with all the consequences like e.g. irradiation of freight consignments and letters and discussions have constantly occupied this Committee since September 2001. Bio-legislation covers a complex area of laws, regulations and guidelines on the international and national levels so that the PQSR Committee is necessarily characterised by vital correspondence and exchange of news. Its self-image and main mission is to function as a mirror reflecting the demands and problems of the Culture Collections on the one hand and of the world-wide scientific community on the other hand. In order to get

more publicity and to demonstrate which issues are addressed by the PQSR Committee, a special flyer was published in August 2002 and widely distributed. The work of the Committee has by no means come to a final point but needless to mention, there are open questions requiring a closer look. This WFCC Committee has been exciting since its foundation and has many challenges ahead of it.

Overview on Main Activities and Milestones

The PQSR Committee was able to fill many issues of its Work Plan successfully with life, some deserve more or constant attention in the future and some certainly beyond measure like e.g. world-wide biosecurity aspects (despatch of dangerous microorganisms/"select agents"/"dual-use" material). A milestone to be highlighted was receiving the WFCC observer status to UNSCETDG and the succeeding positive negotiations on deregulating transport requirements for cultures of Risk Group 2. In order to receive more attention, the PQSR Committee produced a multi-colour flyer describing the main activities, aims and goals and containing the member addresses as well as the WFCC homepage access. Large numbers of this flyer were distributed by the PQSR members on different occasions, at the UN, BTWC Expert Meeting on Disarmament, Geneva, August 2003 and at the UNSCETDG Meeting in Geneva, July 2004.

New Transport Regulations for Infectious Substances as of January 2005

by Dr Christine Rohde

The intention of this information is to briefly inform all shippers of infectious substances on the changes set in force by the **United Nations Model Regulations for the Transport of Dangerous Goods** ("Orange Book"). The UN Sub-Committee of Experts on the Transport of Dangerous Goods, UNSCETDG, agreed on principal changes in the transport regulations for infectious substances, Class 6, Division 6.2. This UN expert group is the relevant international body responsible for defining the packaging and transport requirements of all kinds of dangerous goods. In 2003, WFCC received observer status to this Sub-Committee. The UN Model Regulations are governing packaging and shipping questions for all modes of transport world-wide (road, air, rail, waterways). Air transport plays the major role in case of international shipping of biological materials; therefore the respective **Dangerous Goods Regulations (DGR)** as implemented by the International Air Transport Association (**IATA**) are mentioned here repeatedly. For air transport, the **ICAO Technical Instructions** (ICAO TI, updates every two years) are the legal background whereas the annually updated IATA DGR are regarded as being a user-friendly, actual and reliable handbook for the shipper. It is recommended that all shippers of dangerous goods including infectious substances have access to the IATA DGR, which are available in several languages.

The announced changes appeared for the first time in the IATA DGR 2004 edition as Appendix I and have become effective in January 2005 as chapter 3.6.2 in the IATA DGR 2005 (46th edition). All senders of infectious substances are obliged to use these new regulations when they classify their biological material prior to shipments.

The principal change effective since 01.01.2005 is that the UN Model Regulations moved away from using the Risk Group allocations of microorganisms and that two categories for transport classification of infectious substances apply instead: Category A and Category B. Consequently, the Risk Groups which still play a fundamental role for handling during work with the organisms only play an indirect role for transport classification. The correct classification of dangerous goods or in this context of infectious substances is the very first decision-making step the responsible shipper has to perform before arranging all subsequent steps: choosing the correct packaging and the correct, fastest and safest carrier.

There are fundamental practical differences between the new shipping Category A and Category B: The UN Model Regulations have published an indicative examples list (not shown here) of infectious substances containing highly pathogenic viruses and bacteria classified in Risk Groups 3 and 4. This list is not exhaustive and new or emerging pathogens may be added to it, according to the definition of the criteria for inclusion in Category A (see below). Also, in cases of doubt as to whether or not an infectious substance

meets the criteria, it must be included in Category A. Infectious substances sent under Category A are UN 2814 (affecting humans) or UN 2900 (affecting animals). Such consignments underlie the same regulations, checking and handling procedures, the same documentation requirements and all strict dangerous goods requirements of the transportation chain as shippers of these UN numbers are used to apply, e.g. including the 24 hours emergency contact telephone number on the Shipper's Declaration form and the obligatory advance arrangements between shipper and recipient.

The definition of the new shipping Category A is given under 3.6.2.2.2.1, IATA DGR 2005:

"**Category A**: An infectious substance which is transported in a form that, when exposure to it occurs, is capable of causing permanent disability, life-threatening or fatal disease to humans or animals. Indicative examples of substances that meet these criteria are given in Table 3.6.D."

It is necessary to inform the reader of this information that well-known courier services licensed for transporting infectious substances have placed restrictions on the international transport of the new Category A, UN 2814/UN 2900, which seems comparable to a ban. The transport restrictions are so severe that shippers should have a closer look at the definitions and criteria prior to classification of the infectious substance to be transported:

Classification decisions

Does the definition of Category A apply and does the definition of the term culture apply? What are "high concentrations" in a (freeze-dried) culture compared to a diagnostic sample? Is a freeze-dried culture a true "culture"? The understanding of the *hazard* as mentioned in the definition of Category A excludes the definition of the Risk Group 2 so that it is recommended to classify case by case when organisms allocated to the Risk Group 2 are shipped. What are "diagnostic purposes"? Does it include reference or test strains? All these arguments together have to lead to a justified classification by the shipper who has the responsibility to consider and weigh all these possible hazards. It is recommended to look at the PQSR Committee report (please see WFCC web site).

The definition of the term "Cultures" is given under 3.6.2.1.3, IATA DGR 2005:

"**Cultures** (laboratory stocks) are the result of a process by which pathogens are amplified or propagated in order to generate high concentrations, thereby increasing the risk of infection when exposure to them occurs. This definition refers to cultures prepared for the intentional generation of pathogens and does not include cultures intended for diagnostic and clinical purposes."

The definition of the new shipping Category B is given under 3.6.2.2.2.2, IATA DGR 2005:

"**Category B**: An infectious substance which does not meet the criteria for inclusion in Category A. Infectious substances in Category B must be assigned to UN 3373 except that cultures, as defined in 3.6.2.1.3, must be assigned to UN 2814 or UN 2900, as appropriate."

In case of shipments of Category B, UN 3373, diagnostic specimens, a clear transport deregulation has been verified: a Shipper's Declaration form and a dangerous goods declaration form for road transport (ADR in Europe) are not required. The transport emergency card is not a must anymore. The regulatory bodies have introduced a modification towards a deregulation by introducing the new classification scheme including the new Category system and the new UN number 3373. But, it should be emphasized that

- It is still the shipper who is the responsible person for correct classification of the biological material, packaging, marking and labelling and documentation before offering a consignment for transport (IATA DGR 1.3, 46th ed.)
- The shipper has to be a trained person acc. to IATA DGR 1.5, 46th ed.. Recurrent training is required
- All kinds of infectious substances fall under the transport regulations for dangerous goods, although consignments containing infectious substances classified in Category B, UN 3373, sent for diagnostic purposes, are not accompanied by those documents required for Category A, UN 2814 or UN 2900 resp. (highly pathogenic dangerous microorganisms), their transport is deregulated.
- The correct choice of the required packaging (according to IATA Packing Instruction 650 or PI 602) is crucial. Even if PI 650 packagings are officially sufficient for Category B, UN 3373, PI 602 packagings offer more strength and stability during transport

Non-infectious biological materials:

It is important to note that the UN Model Regulations are NOT governing packaging and shipping of non-infectious biological materials where the definition of a dangerous good does not apply (usually per definition the Risk Group 1 microorganisms). Hence, such microorganisms are NOT regulated by the ICAO TI and IATA DGR. For such biological materials, still the regulations by the Universal Postal Union (UPU) for transport by postal mail services apply. Of course, such substances can also be sent by courier in case national postal services don't permit mail transport of biological materials or if there are other reasons for choosing transport by courier systems. The principal difference between postal mail and courier transport is that the courier transport takes care of the individual consignment and offers tracking of each consignment at any time whereas this is not possible by usual postal mail. Again, it should be mentioned here that if postal mail transport is permitted in an individual case, it is advisable to use registered letter mail instead of normal letter mail. Non-registered letter mail may be used when

freeze-dried harmless biological material is shipped (note: postal parcels are not permitted for transport of any biological material). The Postal Convention (Letter Post Compendium, UPU) contains several Articles describing the international requirements for packing biological materials when sent by Postal mail. These Articles are RE 412, RE 413 and RE 207. Consignments transported by courier services are called freight; they are accompanied by a special document (Waybill).

Whenever microorganisms are shipped and independently of the mode of transport: the **triple packaging system** applies without exemption:

- **Primary receptacle(s)** which have to be leakproof in case of liquid substances
- **Secondary packaging** which has to be leakproof in case of liquid substances
- Rigid **outer packaging** (for better handling, for further protection and for carrying documents, addresses and labels)

A big variety of packagings for all kinds of biological materials (whether they are harmless environmental isolates, diagnostic specimens of Category B or dangerous pathogens of Category A) are offered by specialised manufacturers.

WFCC Resolutions and a perspective of the future

by Dr. David Smith

List of acronyms

ABS	-	Access and Benefit Sharing
ANMD	-	Asian Network on Microbial Research
BRC	-	Biological Resource Centre
BCCM	-	Belgian Co-ordinated Collections of Microorganisms
CABRI	-	Common Access to Biological Resources and Information
CBD	-	Convention on Biological Diversity
CGIAR	-	Consultative Group on International Agricultural Research
CODATA	-	Committee on Data for Science and Technology
ECCO	-	European Culture Collection Organisation
FAO	-	Food and Agriculture Organisation
FORKOMIKRO	-	Communication Forum for Indonesian Culture Collection Curators
GBIF	-	Global Biodiversity Information Facility
GR	-	Genetic Resources
ICCC	-	International Congress for Culture Collections
IPGRI	-	International Plant Genetic Resources Institute
ISBER	-	International Society for Biological and Environmental Repositories
IUBS	-	International Union of Biological Sciences
IUMS	-	International Union of Microbiological Societies
JSCC	-	Japanese Society for Culture Collections
MICRO-NET	-	Microbial Information Network of China
MIRCEN	-	UNESCO Microbial Resource Centers
MOSAICC	-	Micro-organisms Sustainable use and Access International Code of Conduct
MOSAICS	-	Micro-organisms Sustainable use and Access management Integrated Conveyance System
MR	-	Microbiological Resources
OECD	-	Organisation for Economic Co-operation and Development
UKFCC	-	United Kingdom Federation for Culture Collections
UKNCC	-	United Kingdom National Culture Collection
UN	-	United Nations
UNEP	-	United Nations Environment Program
UNESCO	-	United Nations Educational Scientific and Cultural

		Organisation
USFCC	-	United States Federation of Culture Collections, USA
WFCC	-	World Federation for Culture Collections
WHO	-	World Health Organisation
WIPO	-	World Intellectual Property Organisation

One of the key outputs of the World Federation for Culture Collections (WFCC) International Congress for Culture Collections (ICCC) is a list of resolutions of the congress. These identify global issues from discussions and presentations that will form part of the WFCC work Programs between meetings. The WFCC Executive Board and the local ICCC10 Organising Committee supported by the conveners and chairs of the congress drew up a number of resolutions (listed below) as a result of the tenth ICCC held in Tsukuba, Japan. The resolutions address a number of challenges that the culture collections of today face.

A crucial role of a culture collection is to ensure that biological materials are made available for research and confirmation of results. A particular concern is the restricted use of organisms that is being conferred by some Material Transfer Agreements (MTAs) that accompany the transfer of biological materials between, countries, laboratories and scientists. MTAs have been a tool introduced to offer traceability of the movement of genetic resources between providers and users to support the laudable intentions of the Convention on Biological Diversity but which are being used more and more to try and protect Intellectual Property or as conditions of sale. It is the WFCC's view that transfers and use of; in particular, Type Strains should not be impeded by such agreements. The WFCC will continue the work of the Patents Committee under its new work Programs and include practical solutions and common approaches to issues of ownership and IP protection in its future activities. The WFCC is a partner to the European Union funded Project, MOSAICS - Development of a system for appropriate management of access and transfer of microbial resources - Micro-organisms Sustainable use and Access management Integrated Conveyance System. Critical issues in the implementation of the Convention on Biological Diversity (CBD) provisions on access and benefit sharing (ABS) and the derived Bonn Guidelines were addressed by a first phase of this project (further details at the MOSAICC and MOSAICS projects http://www.belspo.be/bccm). There are three main goals of this project. First, it is difficult to assess the economic value of microbial resources (MR). Reliable tools for economic valuation of MR can ease benefit sharing processes and settlement of balanced deals. Secondly, the translation of international rules on ABS at national level induce the multiplication of diverging systems and impede subsequent access and use of MR. A minimum level of harmonisation is necessary. Thirdly, an operational system addressing the issue of ABS must be widely used by a majority of stakeholders to be effective. Advocacy of such a system derived from MOSAICC could foster its implementation by a large number of stakeholders.

A second and very hot topic is biosecurity. Following 9/11 the WFCC was inundated with questions from the press and other media concerning access to dangerous pathogens. As a result action was taken in the form of an

undertaking by WFCC members to adhere to a statement of general guidance. It is evident that the public, Governments and the biotechnology community want further action to ensure that dual use materials do not get into the wrong hands for misuse. The WFCC will endeavour to work with the many players and actors in this field to enable practical and appropriate guidance to be developed and put in place. This issue forms part of general quality management and quality assurance and compliance with national laws and international conventions, rules and regulations. WFCC is already very active in these areas through the activities of its old Postal, Quarantine, Safety Regulations Committee and observer status in the OECD Biological Resource Centre Initiative.

In 1999, the Organisation for Economic Co-operation and Development (OECD) Working Party on Biotechnology endorsed a proposal by Japan to examine support for Biological Resource Centres (BRCs) as a key element of the scientific and technological infrastructure for the life sciences and biotechnology. A report on this initiative was published in 2001, *Biological Resource Centres – Underpinning the Future of Life Sciences and Biotechnology* (http://oecdpublications.gfi-nb.com/cgi-bin/oecdbookshop.storefront). This report argues the need for biological resource centres, strengthened and modified to meet the requirements of the 21st century, and recommended the creation of a Global Biological Resource Centre Network (GBRCN). A second phase prepared documents that laid down the basic rules and mandatory guidance for the participants in the GBRCN. The OECD will complete its development of the instruments required to bring the GBRCN into being, including common operational standards, standards for information linkage and exchange, appropriate security arrangements, guidance on institutional architecture management and on funding, and any necessary interim measures, by 2006 at the latest. The WFCC continues to input into this initiative. It must be remembered that the WFCC published its *Guidelines for the establishment and operation of culture collections* in 1990 and a second edition in 1999 (available via the WFCC web site http://www.wfcc.info) common standards for culture collection operation are not new. Inevitably associated with new requirements and developments is a need for capacity building.

The WFCC has been involved in capacity building from its origins; indeed this is the key function, to share knowledge, information and technologies to help empower scientists in the 'state-of-the-art' maintenance of biological materials and the associated information. It is in the national interest to develop a strategic approach to Genetic Resource (GR) conservation and its legitimate and sustainable use. GR are central to biotechnology, sustainable development and for policy on sustainable agriculture. They are an important tool for meeting a wide range of policy objectives, including protecting the rural environment, promoting sustainable rural economies, promoting sustainable and adaptable farming, promoting sustainable management of natural resources and ensuring high standards of animal health and welfare. Biotechnology will challenge many aspects of our life as profoundly as information technologies. The WFCC offer training courses many associated with their International Congress for Culture Collections held every 4 years up

to 2004 and the next is to be held in Goslar, Germany in 2007 (http://www.wfcc.info). The courses are normally general in nature covering management of culture collections and preservation of organisms. Member collections of the WFCC offer individual training, often tailor-made to requirements. Although the WFCC has a mandate from its members to co-ordinate activities to date it has not done so, it provides *ad hoc* training as requested in addition to the courses associated with its meetings. It held two training courses on the occasion of ICCC9 in Brisbane and similar courses were held at ICCC10. A training course to support collections in Morocco was held in Rabat in 2004, and special workshops are often arranged for example on *Microbial resources and biodiscovery* held in Melbourne, Australia in 2003. Such courses will continue but there is a need for co-ordination and a training strategy to be linked to facility establishment and enhancement and to national needs. The WFCC will work with donors and other initiatives to help get the best of such training initiatives and continue to make a difference.

There are many initiatives and projects that are underway that offer the culture collection community opportunities but we do get confused as we are bombarded by acronyms, a few of which are listed above that are used in this text. One collection, an individual scientist or even a research group struggles to keep pace with all these activities and importantly contribute and try to ensure that there is no duplication of effort. The WFCC will consolidate and develop the existing links to OECD (BRC task force), GBIF, UN, WIPO, UNEP, CBD, IUMS, IUBS, UNESCO, CODATA. Create new linkages to other international organisations e.g. WHO, FAO, IPGRI, CGIAR, ISBER. The WFCC will also endeavour to involve national and regional organisations of Culture Collections to enhance collaboration in WFCC actions. We will promote the awareness and use of member expertise. There are several national and regional collection federations and organisations to which WFCC members belong and through which the WFCC should collaborate to support local activities and developments. A number of these organisations are adherent to the WFCC and therefore should collaborate to achieve common goals. Examples of such Federations/Societies/Networks are:

- ANMD Asian Network on Microbial Research
- CABRI Common Access to Biological Resources and Information
- BCCM Belgian Co-ordinated Collections of Microorganisms
- ECCO European Culture Collection Organisation
- Indonesian Network of Culture Collections
- JSCC Japanese Society for Culture Collections
- MICRO-NET Microbial Information Network of China
- MIRCEN UNESCO Microbial Resource Centers
- Portuguese Network of Culture Collections
- UKFCC United Kingdom Federation for Culture Collections
- UKNCC United Kingdom National Culture Collection
- USFCC United States Federation of Culture Collections

These and potential new networks have a role to play with the WFCC in raising public awareness. It is imperative that the public see the beneficial

side of microbiology at time when they are bombarded with the negative side of new emerging disease, bioterrorism and invasive alien species. The WFCC have a new work Program on visibility that will work with others to get the right messages out there with impact. Collections must now deal with the vast diversity of new genetic entities generated by life scientists as they seek to reveal the genomes of many organisms and to engineer new cells with novel properties. Genomics leads to the amplification of biodiversity in the form of clones containing fragments of whole genomes. Sequencing the genome of a single human cell generates tens of thousands of new entities (*e.g.* yeast containing fragments of the human genome) that need to be conserved and distributed by BRCs. Similarly, each bacterial cell sequenced means hundreds of such new entities to be preserved (OECD, 2001). There are a number of initiatives in this area and some information generated is erroneous. The WFCC will work with genome projects and genome database providers to improve the quality and validity of genomic data placed in the public domain.

There is so much to be done. The WFCC relies on the activities of its members to address these issues. It will prioritise its work and produce a business plan to co-ordinate and ensure output from these intentions. This plan will be available in 2005 and will be posted on the WFCC web site for your input and comment. It will not be laid down in 'tablets of stone', business plans never are, it will need to be flexible to react to new problems, opportunities, information and available funding. The plan will put activities in place to implement the following:

ICCC10 resolutions

1. Type strains must be regarded as the property of the international scientific community and must be made available to qualified workers without restrictions or impediment imposed by MTA.
2. WFCC will facilitate workable solutions to implement the CBD.
3. WFCC will seek harmonized technical and management measures to address the issue of biosecurity.
4. WFCC will take a leading role in the development of Biological Resource Centre (culture collection) operational standards and work with international organisations and initiatives to establish capacity building Programs.
5. WFCC will endeavour to represent its members in all key international initiatives that impact on the operations of culture collections e.g. CBD, GTI, GBIF, CODATA, OECD, UN organisations, WHO, UNESCO, WIPO, etc.
6. WFCC works closely with the microbiological societies and industry to improve public understanding of the value of the micro-organisms and their impact on human, animal, plant and ecosystem health.
7. WFCC will work with genome projects and genome database providers to improve the quality and validity of genomic data placed in the public domain.
8. WFCC undertakes to set up a strategy to develop networks on a geographical or a thematic basis, encouraging culture collections to start

or to join initiatives with the aim to enhance communication and collaboration.

9. The time period between International Culture Collection Congresses is too long as science, technology and regulatory environment change so quickly. It is therefore agreed that the time between ICCC 10 and ICCC 11 be reduced to 3 years.
10. WFCC will draw up a business plan.
11. The WFCC committees are dissolved and replaced by work Programs under the direct guidance of the Executive Board.

The next ICCC will be in 2007, a reduction in the gap between these extremely important WFCC events. We must improve our communication and joint activities between congresses and the WFCC will be proactive in engaging members and other partners to get its valuable work done.

WFCC Work Programs

To enhance and more clearly prioritise the work of the WFCC the Executive Board has agreed that work Programs would be established to replace the old committee structure. Executive Board members have volunteered to lead these Programs to give better linkage between the Board and the work of the WFCC. This mechanism will not destroy the huge success that some of these committees have had in the past. It is envisaged that some will be more effective. These work packages and the leaders were selected as below:

- Postal, quarantine and biosafety regulations: Christine Rohde
- Quality matters: David Smith
- Information Technology: George Garrity
- Biodiscovery: Ipek Kurtböke
- Endangered Collections: Peter Green
- Capacity building: Jean Swings
- Intellectual property and ownership issues: Philippe Desmeth
- WFCC visibility: Erko Stackebrandt
- World Data Centre for Microorganisms: Hideaki Sugawara
- Newsletter: Ipek Kurtböke

Details on the key objectives of these work Programs will be provided as they become available, some of which are outlined below:

Quality Matters Work Program (ECWP) (Contact: Dr David Smith)

The WFCC will work closely with the OECD Biological Resource Centre Task Force (BRCTF) and other relevant organisations such as the International Society for Biological and Environmental Repositories (ISBER) in the development of appropriate standards for the operations of culture collections. Particularly it will work with the OECD BRC Task Force to:

- Assess the impact of the general and domain specific standards developed by the OECD BRCTF
- Standard for the operation of Biological Resource Centres (BRCs) - DSTP/STP/BIO(2003)13: declassified
- Micro-organism Domain Specific Standard DSTP/STP/BIO(2003)20
- Domain specific criteria for animal, plant and human-derived material
- Institutional requirements for the GBRCN DST/STP/BIO(2003)15
- Financial aspects of BRCs DSTI/STP/BIO(2003)16/REV1
- Examine the different mechanisms of certification/accreditation recommended by the BRCTF.
- Accreditation of Biological Resource Centres (BRCs) - DSTI/STP/BIO(2003)12: declassified
- Test the implementation of the principles of biosecurity, ownership and management of IP through MTAs and other mechanisms and as such work closely with the EU projects MOSAICS and the Postal, quarantine and biosafety regulations work Program.
- Biosecurity DSTI/STP/BIO(2003)22

- Investigate mechanisms for exchange of material, which must meet the OECD mandatory guidelines in close collaboration with the Intellectual property and ownership, issues Work Program.

The QMWP will, taking into account the above, revise the WFCC Guidelines on the establishment and operation of culture collections and, in close collaboration with the Capacity Building Work Program, address the capacity building needs to put in place appropriate mechanisms for these quality management procedures.

Endangered Collection Work Program (ECWP) (contact: Dr Peter Green)

- To provide a focal point or first port of call for any collection (industrial/private/academic) which considers itself to be endangered or in need of help or advice with respect to its future sustainability.
- To assess the requirements of endangered collections who seek assistance and to provide any support, advice or practical help to facilitate the continued survival of that collection; preferably in situ.
- In the event of a culture collection being in imminent danger of being lost, to visit, or by means of correspondence, assess the holdings of that collection and attempt to find an alternative home for all or part of said collection.

1. To seek additional levels of funding to build upon those achieved previously.

This will be achieved by developing a sustainable funding strategy document looking at the following areas of funding aimed at supporting the goals of the ECWP:

- Attempt to increase amount of award of grant aid from existing sources (currently the Society for Applied Microbiology - SfAM).
- Exploiting to the full other available indirect funding sources periodically e.g. the SGM International Development Fund.
- Contacting existing charitable organisations as potential new funding sources.
- Heightening awareness of new research projects at the drafting stage in order to persuade the authors to consider provision for the maintenance of cultures arising from the project and help with infrastructure provision with the local/regional collections whose task it is to maintain said organisms.
- To make use of the regional distribution of ECWP members who can try to lobby for special funds within their country or region to set up complimentary funds to the SfAM Endangered Culture Collection Fund. Ideally these funds should be regional or global in scope of usage.
- Locating and exploiting any additional sources of International funding, which may be available to developing countries?

To work more closely with complimentary groups or interested parties both within and out with the WFCC to the benefit of endangered or potentially endangered collections.

- Specifically to work with the WFCC education and capacity building task group whose role may overlap with some of our own initiatives or calls for assistance e.g. in countries where there is poor or no co-ordination/communication/training between disparate groups within that country or region.
- To investigate the possibility of “twinning” in order that an established culture collection can offer one-on-one assistance to an endangered collection if that appears appropriate or helpful.

Biodiscovery Work Program (contact: Dr Ipek Kurtböke)

Biodiscovery is based on search for exploitable and diverse biological resources. In this search the screening of microbial natural products still continues to represent an important route to the discovery of novel chemicals for development of new therapeutic agents, and the evaluation of the potential of lesser-known and/or new bacterial taxa is of increasing interest. However, selection of novel bioactive producing microoorganisms from nature requires a sound microbial taxonomical knowledge and fuller understanding of microbial ecology and physiology as means for revealing novelty. Therefore, taxonomic expertise combined with Microbial Genetic Resources Networks will provide a stronger platform to novel discoveries.

The current work program involves the following:

1] Stress the importance of the economic value of microbial diversity with reference to the CBD and making recommendations towards global regulations on access and benefit sharing;

2] Improve understanding towards the needs of the key players and establishment of common grounds between the public sectors, private sectors, intermediaries, communities involved in the chain of biodiscovery;

3] Overview of training schemes and methods used during the building of the source-country’s institutional capacity in relation to scientific and technological trends;

4] Overview of conservation policies and wise-management of global resources and benefits associated with the use of traditional knowledge;

5] Focus on social, environmental and ethical issues and the need for the conservation of microhabitats;

6] Organization of workshops and special sessions on the current program during the WFCC Congresses and facilitation of networking among the interested parties.

Postal, Quarantine & Safety Regulations Work Program (contact: Dr Christine Rohde

The new Work Program on postal, quarantine and biosafety regulations replaces the former WFCC PQSR Committee. It is one of nine new Work Programs agreed during ICCC-10, Tsukuba, October 2004. The responsible person leading this Work Program is Christine Rohde, DSMZ. The title of the former Committee (PQSR) is retained to make the main objectives of this Work Program clear. Furthermore, this WFCC Committee is recognised externally through several successful activities. The plan presented below is a basis for new or continuing activities. The Work Programs are designed to remain flexible and to react to new problems, opportunities and information as agreed by the WFCC Executive Board.

Following the Congress in Tsukuba, October 2004, the following collaborators have volunteered to be active members of this Work Program:
Chantal Bizet, Barry Holmes, Pat Short, Lirong Song, Masako Takashima, Claudine Vereecke, Vera Weihs, Christine Rohde, Lynne Sigler.
More colleagues are very welcome to actively collaborate.

Areas of Concern for Future Activities (based upon PQSR Committee report, 2004)

- International comparison and harmonisation of Risk Group allocations
- Regular information dissemination on inclusion of new species in the Risk Groups
- Educational outreach (on the distribution of pathogens)
- Developing a Code of Conduct re. biosecurity together with international initiatives and societies
- Addressing Ethics questions related to the handling and distribution of whole organisms and cells
- Improvement of data release concerning PQSR questions
- Preparation of lists of organisms for inclusion in the new transport Category B

Work Program to address areas of concern and WFCC priorities

Regulations and best practice for the transport of cultures

1. The new IATA Dangerous Goods regulations categorise organisms for transport into Category A and B. The Work Group will draft suitable lists and assess recent changes in practice by couriers who are refusing to transport Category A, infectious substances UN 2814 and UN 2900.

Biosecurity and culture collections

2. The WFCC must take a responsible stand on biosecurity issues and work with appropriate international bodies to ensure best practice is adopted

by cuture collections. The Work Group will work with groups such as the OECD, BRC Initiative/Working Party on biosecurity and other WFCC work Programs to ensure that the WFCC disseminate the right messages re. biosecurity.

WFCC representation at international initiatives (here: OECD, UN, WHO)

3. The work Group will provide WFCC representation at OECD, UN organisations and the WHO (among others). Representation at OECD and UN (UNSCETDG and UN Biosecurity/Bio-weaponry disarmament initiatives) have already been established and these will be maintained. The Work Group will also look for opportunities for the WFCC to get involved proactively in a wide range of policy issues including that of ethical considerations regarding culture collection activities.

4. Additionally, the Work Group will compare the different allocations of microorganisms to the Risk Groups and identify opportunities for harmonisation. Appropriate mechanisms for the inclusion of newly described species will be explored. The Work Group will advise WFCC member collections on best practice, how to establish courses, workshops, and individual training and how to address questions (publications, homepage information incl. FAQ pages) in areas of transport, safety, and compliance with legislation. These issues and that of biosecurity in particular, should be raised with national and international microbiological societies e.g. IUMS, to ensure not only collections are aware but microbiologists are clear on their responsibilities. There is the potential to design a Code of Conduct. The Work Group will continue its efforts to gather and distribute data on PQSR issues.

Biodiscovery to Improve Human and Environmental Health
at the
Institute for Sustainability, Health and Regional Engagement
http://www.usc.edu.au/ishare

by Dr Ipek Kurtböke

The screening of natural products continues to represent an important route to the discovery of novel chemicals for development of new therapeutic agents, and for this reason the evaluation of the potential of lesser-known and/or new plant and microbial taxa is of increasing interest. Australia appears to be a "hot spot" for the search and discovery of novel compounds, as it is one of the world's most biodiverse continents. Australia has been geologically separated from other continents for over 20 million years, which has allowed a period of extensive evolutionary divergence. As a result, Australia has a high rate of endemism in both its flora and fauna.

An increasing understanding of emerging ecosystem health issues such as antibiotic resistance in pathogenic organisms and the need to replace toxic agrochemicals with pest specific agrobiological compounds provides one of the research foci of the Institute for Sustainability, Health and Regional Engagement (iSHARE): "Biodiscovery to improve Human and Environmental Health". The focus also extends to the discovery of novel and stable enzymes from Australian biological resources to the breakdown of urban and agricultural waste, bioremediate tannery and paper industry waste, as well as the use of these enzymes in detergents, food and in leather and textile manufacturing.

iSHaRE is located at the University of the Sunshine Coast in southern Queensland, Australia. It is a university-wide research institute dedicated to enhancing human and environmental well being through research, research training and regional engagement.

iSHaRE's objectives are to:

- Support fundamental and applied research in the environment and health fields
- Support the practical application of research findings
- Provide research and consulting services to promote sustainable regional development and communities
- Establish innovative, collaborative and cost-effective support systems for research, the gathering of market intelligence, information dissemination and spatial information management

Research Programs and Areas of Strength

Research within iSHaRE is undertaken in one of two Research Programs. These are subdivided into a number of Areas of Strength, which are multidisciplinary teams focusing on an area of research. Research Programs are identified as:

Healthy People - Sustainable Communities

Human activities at both individual and community level modify biophysical and socio-economic environments, and the interactions between them, in turn, impact on health. The Healthy People - Sustainable Communities research program acknowledges this complexity. It features both in-depth, discipline-based inquiry and broad-based, transdisciplinary research that addresses the health of individuals, populations, communities and ecosystems.

Researchers within the Healthy People - Sustainable Communities Program have five Areas of Strength:

- Individual Physiological Health
- Environmental Epidemiology
- Sustainable Community Development
- Biodiscovery to Improve Human and Environmental Health
- Public Health Nutrition

Sustainable Environments

The Sustainable Environments research program builds on the philosophy of ecologically sustainable development (ESD), broadly encompassing the physical, biological, economic and social conditions of all life forms. The program is focused on the development of integrated management systems that ensure the maintenance of three critical components of ESD- biodiversity, ecological integrity, and natural capital.

Researchers within the Sustainable Environments Program have six Areas of Strength:

- Sustainable Production Systems
- Biodiversity, Conservation and Restoration
- Sustainable Tourism
- Environmental Planning and Management
- Environmental and Climate Change
- Estuarine, Coastal and Ocean Research

These Research Programs are transdisciplinary, have strong international track records and focus on research that is relevant to rapidly developing coastal regions.

<u>Consultancy Services</u>

iSHaRE provides a range of consulting services as part of its commitment to regional engagement. Consultancy Services include:

- Ecological footprint analysis
- Triple bottom line / sustainability reporting
- Input-output analysis

- 'Off-site' environmental impact assessments
- Sustainable tourism assessments
- Community health studies
- Environmental epidemiology
- Waste management
- Geographical Information System (GIS) services

Research Facilities

iSHaRE facilitates environmental and health research through the provision and management of research facilities at Fraser Island and Beerwah, just north of Brisbane in Queensland. Collaborative researchers, both nationally and internationally, are able to access these facilities on the same generous terms as those provided to academics at the University of the Sunshine Coast.

Fraser Island is a World Heritage Area located off the southern coast of Queensland. It is a complex ecosystem of sand dunes, lakes and subtropical forests that grow solely on sand, and is an outstanding global example of continuing biological and geological processes. Over 120 kilometres long and over 22 kilometres across at its widest point, the Island has developed over 800,000 years and is both a unique natural environment and an ideal location for scientific research.

The Fraser Island Research and Education Facility includes a number of sites:

- ***Kingfisher Bay Research and Education Facility:***

This facility is located at Kingfisher Bay Resort and Village, and is used for advanced level environmental and eco-tourism research, and education (primarily for rangers and university groups). The facility provides a well-equipped open-plan teaching room, a laboratory for basic environmental research, refrigerator and freezer rooms, a small office and library, and a specimen receiving deck. Accommodation for researchers and graduate students is also available.

- ***Dilli Village Environmental Education Camp*:**

Dilli Village is an environmental education camp for secondary and tertiary level students, located on low sand dunes 400 meters from the beach. Dilli Village provides an eco-edu-tourism experience for island visitors. The Village provides accommodation for students and staff, education programs (arts, business, eco-tourism and science) and access to field study sites for primary, secondary and tertiary student groups. Researchers and groups with genuine environmental interests in the region are encouraged to use the site. Additionally, Dilli Village welcomes private individuals such as family groups, day visitors and small group tours. The accommodation consists of a range of cabins, bunkhouses and camping spaces.

- ***Beerwah Field Study Facility:***

The Beerwah Field Study Facility is located among the Glasshouse Mountains at Beerwah on the Sunshine Coast in Queensland, 100 km north of Brisbane on the eastern seaboard of Australia. The area fringes the RAMSAR-registered Pumicestone Passage, other national parks and is surrounded by state-managed forest. The site is also of significant geologic and cultural importance, surrounded by a complex mix of urban settlement and rural industries, including forestry, pineapple and macadamia. The facility provides accommodation facilities (both dormitory and camping), basic support services for environmental fieldwork and research, resource materials associated with both secondary and tertiary teaching, and a meeting place for environmental community groups.

Linking the Priority Research Areas of the iSHaRE and the WFCC

Past WFCC President Professor Jean Swings visiting iSHARE (4th October, 2004) with iSHARE staff members (from left: Assoc. Prof. Pam Dyer (Program Director), Assoc. Prof. Ron Neller (iSHaRE Director), Dr Ipek Kurtböke (Biodiscovery Strength Area Coordinator), Mrs Satu Stephenson (Executive Officer) and Miss Julie Waldron (Project Officer)

Professor Jean Swings, past-President of the World Federation of Culture Collection and Head of the Microbiology Department at the University of Gent, Belgium visited iSHaRE as part of his collaboration with Dr Ipek Kurtböke and to launch a new book titled *Microbial Genetic Resources and Biodiscovery*, Dr Kurtböke and Prof. Swings have co-edited. This is a joint publication of the WFCC and iSHaRE, and includes 16 chapters in the fields of microbial genetic resources, biodiscovery and intellectual property rights, bioinformatics and functional genomics, search for bioactive compound producing microorganisms, taxonomy and culture collections.

Currently iSHaRE's Program structure includes strength areas such as Biodiscovery to Improve Human and Environmental Health, Biodiversity,

Conservation and Restoration. During his visit Prof. Swings, upon observing similarities between the strength areas of the two organizations, recommended that parallel programs should be established to encourage further collaboration. His recommendations were received favourably during the General Assembly of the Federation and a work program titled *Biodiscovery* has been established under the WFCC umbrella.

The New Zealand Reference Culture Collection, Medical Section

by Patricia F. M. Short

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WHAT WE ARE

The New Zealand Reference Culture Collection, Medical Section (NZRM, World Data Collection No. 457) is an important service collection for microbiologists in New Zealand, supplying the country's hospital and community laboratories and science workers in education, research, manufacturing and quality control laboratories.

The NZRM began life as a small collection of medical interest in 1955 at Wellington's National Health Institute. The Collection's first ampoules were prepared on a homemade freeze drier, which had a silica gel column with 30 ampoule attachments. The vacuum pump achieved a reasonable vacuum, but there was no centrifugation so the cell suspension usually ended up on the cotton wool plug! We still have ampoules made in those days, great care is taken when opening them, as many are still viable, especially the hardier enteric organisms.

The Institute moved in 1982 to a new purpose-built building in nearby Porirua and the Collection has grown steadily over the years to its present size of 4300 accessions.

The NZRM is funded principally by Government health agencies and supported by ESR, a Crown Research Institute, whose resources include specialist reference laboratories where the Collection is based. These laboratories have expertise in bacteriology and virology identification, and established alliances with other New Zealand reference laboratories assist us in maintaining our mycology and anaerobe accessions.

SERVICES

The majority of accessions are supplied as freeze-dried ampoules. Our current freeze-dryer is a Thermo Savant ModulyoD, which is based on the Edwards freeze-dryer, we used previously, and batch capability is 96 0.5ml ampoules.

A catalogue is issued which lists the bacteria, yeasts and fungi held; many of these are internationally used reference strains. The catalogue is available as a paper document and is also viewable on our website www.esr.cri.nz.

In addition to the supply of strains the NZRM provides an identification service using both phenotypic and molecular methods. Our 16S rRna gene sequencing of unusual isolates in recent years has identified several recently described genera and species of significance in human health. Examples are *Pandoraea* species (*pulmonicola, pnomenusa* and *sputorum*) and *Inquilinus limosus* from cystic fibrosis patients, and *Corynebacterium riegelii* and *C. coyleae* from blood cultures. New species such as these are added to the Collection as examples of New Zealand biodiversity.

SAFETY AND SECURITY

The NZRM holds cultures of Risk Group 1 and 2 only as our laboratories are approved to Physical Containment (PC) level 2, and the collection is stored in secure buildings.

To guard against loss due to the hazards of earthquakes (a real possibility in New Zealand!) and fire, safety stock of all accessions has been stored in a heat and shock-proof data safe in a separate building.

Cultures are supplied only to laboratories (not private addresses), to bona-fide approved requestors. Documentation, packing, and labelling used are in accordance with the IATA Dangerous Goods Regulations and shipping is by traceable courier.

REGULATORY CONTROLS

The advent of the Hazardous Substances and New Organisms (HSNO) Act in New Zealand in 1996 has encouraged the deposition of representative strains of indigenous species in the NZRM and other New Zealand Collections. The HSNO legislation controls the importation and holding of “new” organisms i.e. those not known to be present in the New Zealand environment, so it is important to be able to determine if a particular species is found here.

The NZRM has been designated as an approved “Containment Facility for Microorganisms” so we are able to hold Risk group 2 organisms, including new and genetically modified organisms. The approval is granted by the New Zealand authority responsible for biosecurity, the Ministry of Agriculture and Forestry (MAF).

CONCLUSION

The NZRM is a valuable reference collection for New Zealand scientific workers. Much knowledge and experience has been gained through achieving and maintaining compliance with legislative and biosecurity requirements. The difficulties now encountered by New Zealand workers wishing to import, transport, or work with, organisms have led to the increased importance of the Collection (and other New Zealand collections) as a source of strains, identification services, expert advice and assistance.

ESTABLISHMENT AND MAINTENANCE OF FUNGAL CULTURE COLLECTION FOR FUNDAMENTAL AND APPLIED MYCOLOGICAL AND BIOTECHNOLOGICAL RESEARCH IN ARMENIA

by Prof. Suzanna M. Badalyan

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Biological Resource Centers (BRCs) of different living organisms constitute an essential part of the scientific and technological infrastructure of life sciences and biotechnology. They are intended for preserving the natural resources and making them available for both fundamental and applied biotechnological research [21]. The BRCs contain Culture Collections (CC) and databases of cultivable organisms providing information relevant to these collections and bioinformatics.

Establishment and maintenance of CC of different groups of fungal organisms (*Zygomycetes, Ascomycetes, Basidiomycetes, Deuteromycetes,* etc) is both the way of preserving the fungal biodiversity and following their development processes by conservation *ex situ*.

Recently, the interest towards higher fungi (mushrooms) as a source of valuable food, bioactive metabolites and enzymes has grown up [3-5, 24, 27]. Their active metabolites possess a large spectrum of therapeutic action, such as antitumor and immune-modulating [3, 23, 26], antibacterial [14], antifungal [9], antioxidant [8], antiprotozoal [10], hypoglycemic [7, 22, 25] etc. Mushroom cultures can be quite valuable in obtaining novel bio-pharmaceuticals and functional food additives, as well as enzymes with thrombolytic, fibrinolytic and milk-coagulating activities and be used in medicinal and food industry [16, 28].

Armenia is situated in the mountainous region of South Caucasus. It occupies an area of 29.9 km2. The neighbor countries are Georgia, Azerbaijan, Turkey and Iran (Fig. 1). The climate is humid in the northern and dry continental in the southern regions of Armenia. Around 1500 mushroom species have been described in Armenia. Among them about 285 are edible, 60 poisonous and more than 60 species possess medicinal properties [2, 6, 19].

Fig 1: Geographic location of Armenia

The main goal for establishing specialized fungal culture collection (FCC) in Armenia is the realization of fundamental and applied mycological and biotechnological research at local, regional and international levels. It will also assist in the development of mushroom industry in Armenia.

The establishment of FCC was initiated by Prof. Dr. S.M. Badalyan at the Yerevan State University (YSU). Presently, the collected fungal strains are preserved at the Fungal Biology and Biotechnology Group (FBBG, YSU) led by S.M. Badalyan and consist of around 388 living strains belonging to 114 species and 59 genera of macroscopic and microscopic fungi.

The FCC includes 60 species and 241 strains of macroscopic fungi (*Basidiomycetes, Ascomycetes*). Among these, 35 species and 197 strains possess known medicinal properties, 27 species are edible and 3 are poisonous. Most of the mushroom cultures were isolated from Armenia, however several strains were obtained from other institutions (Lomonosov Moscow State University, Russia; Kholodny Institute of Botany, Kiev, Ukraine; University of Toulouse France; Bologna University, Italy; Catholic University of Leuven, Belgium; University of Göttingen, Germany and Duke University, USA). The *Flammulina velutipes, Pleurotus ostreatus* and *Coprinus* spp. collections are represented by a wide diversity of strains.

In 1999, the establishment of CC of filamentous fungi was started in collaboration with Dr. Jean Mouchacca (Museum Nationale d'Histoire de Nature, Paris) and Dr. Gloria Innochenti (University of Bologna, Italy). Our collection includes 142 strains and 54 species of filamentous fungi from 30 genera (*Zygomycetes, Ascomycetes, Deuteromycetes*). Among them 11 species 101 strains are keratinophilic (potentially pathogenic for humans and animals), 14 species and 16 strains are phytopathogenic and their antagonists (*Trichoderma* spp., *Gliocladium roseum*, etc.).

Preservation of cultures. The fungal cultures are preserved in refrigerator at 4-5◦ C on agar medium. Several mushroom strains are preserved in the distilled water. During every renewal, the cultures are quarterly checked for purity and stability of morphological patterns by microbiological methods. However, it is an expensive culture preservation method. Therefore, elaboration and application of modern culture preservation facilities, such as liquid nitrogen cryogenic storage, lyophilization and other drying techniques are needed.

Presently, investigation of morphological, ecological and physiological characteristics of fungal cultures is actively carried out at the FBBG of YSU in collaboration with University of Tennessee (USA), Göttingen and Jena Universities (Germany), Bologna University (Italy) and Museum Nationale d'Histoire de Nature (Paris, France).

Morphological and ecological screening of cultures: Investigation of macro-, micro-morphological peculiarities and growth characteristics of mycelia (colony morphology, growth rate and coefficient), elaboration of optimal vegetative growth conditions have been estimated using different nutrient media, stationary and submerge cultivation methods under different temperature (from 5 to 37^{o}C) and pH (from 3 to 14) conditions [14, 15, 20, etc.].

Genetic identification of cultures: ITS-rDNA nucleotide sequence analyses were carried out in collaboration with Prof. Karen Hughes (Mycology Lab, Tennessee University, USA), Prof. Ursula Kües (Department of Molecular Wood Biotechnology, University of Göttingen, Germany) and Dr. Karol Szafranski (Laboratory of Genome Analyses, Jena University, Germany). Presently, our FCC consists of 24 species and 104 strains of genetically identified macroscopic fungi [17].

Myco-pharmacological research. Around 28 species and 60 strains with known medicinal properties (*Ganoderma lucidum, Schizophyllum commune, Flammulina velutipes, Coprinus comatus, Pleurotus ostreatus,* and others) are gradually getting involved in our current Medicinal Mushrooms Myco-Pharmacological Screening Program (MMMPHSP). Further investigation of mushroom cultures will assist in production of new mushroom-based bio-pharmaceuticals/dietary supplements with health-enhancing effect [8, 10, 28].

Medical mycology and phytopathology. Maintenance of FCC will assist in progression of other aspects of our recently started research in medical mycology and phytopathology (keratinophilic fungi, fungal infections of humans, animals and plants, antifungal agents, etc.) [12, 13, 18].
Further extension of taxonomic and eco-geographical diversity of collected species/strains, genetic identification of cultures, digitalization and creation of information Database (DB) accessible to the international scientific community and publication of FCC catalogue are in progress.

Acknowledgement

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EX -SOVIET DEVELOPMENTS IN THE ELIAVA INSTITUTE OF BACTERIOPHAGE, MICROBIOLOGY AND VIROLOGY A WORLD PREMIER INSTITUTE IN BACTERIOPHAGE RESEARCH

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Introduction

At the beginning of the 20th century d'Herelle suggested that bacterial viruses (bacteriophgaes) might be applied to the control of bacterial diseases. In the West this idea was explored in a desultory fashion only and was eventually discarded largely due to the advent of extensive antibiotic usage. However, interest was maintained in the countries of the FSU where bacteriophage therapy has been applied extensively since that time. Central to this work was the Eliava Institute of Bacteriophage, Microbiology and Virology in Tbilisi, Georgia, which was founded thanks to joint efforts of two professors George Eliava and Felix D'Herelle (Fig. 1). This institute remained continuously active in this field for more than 75 years.

Figure 1. Dr. Elena Makashvili (left), Professor Felix D'Herelle (in the centre), Professor George Eliava (right). Photo is taken in 1934 in Tbilisi, Georgia.

Vast collections of prophylactic and therapeutic phages have been gathered during the long history of the institute.

In the Eliava IBMV, phages were sought for bacterial pathogens implicated in disease outbreaks in different parts of the SU and were dispatched for use in hospitals throughout the country. Although infections caused by a wide variety of bacterial pathogens have been treated, much of this has been published in Russian and is not readily available in the West. By contrast, interest in the West has been limited to a small number of enthusiasts and academics and until very recently there has been little interest. The main

reason that the medical and scientific communities are now beginning to take notice, is the continuing world-wide rise in the incidence of multiple-antibiotic-resistant bacterial pathogens and the absence of effective means for their control.

The present report summarizes previous experience of use of bacteriophages in medicine as developed in the FSU countries.

The principle activities of bacteriophage relevant to their application in therapy

Bacteriophages are viruses for which bacteria are the natural hosts. There are two main groups of bacteriophages – **temperate** and **intemperate**. The initial stage of infection for both groups is an adsorption of an individual phage particle to a susceptible bacterium. This occurs usually through the interaction between the phage tail and a specific attachment molecule on the related bacterial surface. The phage injects its nucleic acid into the cell where it replicates itself (Fig. 2).

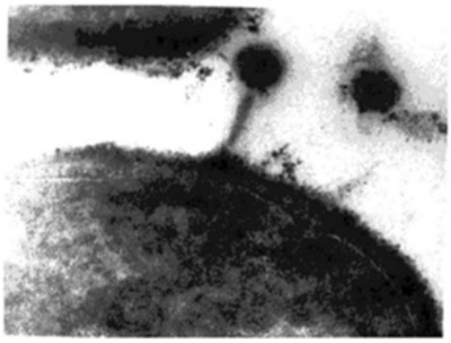

Figure 2. Attachment of the phage Sb-1 to the surface of *S. aureus*

The temperate phages form stable relationship with the host cell, which maintains for many generations. Replication of intemperate phages results in formation of the mature particles around the newly synthesized phage nucleic acid followed by lysis of the cell and release of the new daughter phages (Fig. 3).

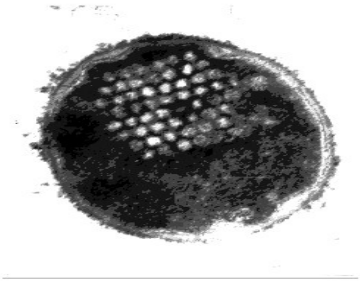

Figure 3. Propagation of a virulent bacteriophage Sb-1 inside *S. aureus* bacterial cell.

The whole idea suggested by D'Herelle in early 1920s involves the exploitation and application of a biological system that is already in operation naturally and for which there is good evidence as to its ability to determine the outcome of natural and experimental infections. Thus, it is likely that the conditions exist under which the system operates optimally and all attempts must be made to reproduce these conditions to achieve optimal activity.

Clinical efficacy of bacteriophages in therapy and prophylaxis: experience from the Eliava Institute for Bacteriophage, Microbiology and Virology (IBMV)

Reviewing the old Soviet literature it becomes obvious that the mass application of bacteriophages was first facilitated in relation to the Finnish campaign (1938-1939) and then during the Second World War (1941-1945). The period between 1930s and 1940s coincides with the peak of a number of scientific publications on phage therapy. Hence, it is sometimes difficult to find access to the old data. This, in part, explains why most of the results of the clinical experiments are not properly designed and registered and the fact that the data for the control groups often are missing. Migration of the patients from a frontline hospital to the base one did not allow the doctors to accomplish a proper monitoring of the clinical effect of phage therapy. However, the period of war and lack of therapeutic preparations inspired the Soviet doctors to perform the new trials with phages and invent the novel methods for their administration. Ironically, this period turned into a genuine heyday for a creative search in the field of phage therapy.

The first mass experiment - prophylaxis of gas gangrene during the Second World War

Kokin (1947 - cited in Krestovnikova, 1947) describes application of the mixtures of anaerobic, *Staphylococcus* and *Streptococcus* phages (produced by the IBMV, Tbilisi, Georgia) for treatment of gas gangrene in soldiers. The mixture was applied to 767 cases and resulted in a decrease of the death rate to 18.8% instead of 42.2% in the control group treated with the traditional methods. The other group of authors have observed the low death rates of 19.2% in the group of soldiers treated with the same mixture of phages against 54.2% treated with other medications (Lvov, Pasternak, 1947 - cited in Krestovnikova, 1947).

In addition to therapy, this phage mixture has been used by the mobile sanitary brigades as an emergency aid for treatment of wounds (prophylactics for gas gangrene) (Krestovnikova, 1947). This paper summarizes the observations of the three mobile brigades. Observation was carried out within 2-6 weeks in course of the evacuation of the patients from the front-line hospital to the basic one. In the first group counting 2500 soldiers and treated with phages, only 35 (1.4%) showed the symptoms of gas gangrene. In the control group of 7918 wounded solders, 342 (4,3%) were infected. The second brigade applied phage therapy to 941 soldiers, only 14 (1.4%) of which were infected with gas gangrene, in comparison with 6.8% from the control group treated with other methods. The third brigade dealing with 2584

solders observed the development of the disease in 18 soldiers (0.7%) while in the control group, the disease has emerged just in 2.3% of cases. Comparing the data described by the three independent brigades it becomes apparent that the 3-fold decrease of incidence of the cases with gas gangrene is a direct consequence of the application of phage mixtures for prophylactic treatment of wounds (Krestovnikova, 1947).

Treatment of the deep forms of dermatitis caused by Staphylococcal infection

Bacteriophage therapy of the deep forms of dermatitis resulting from Staphylococcus was shown to be effective and is described in a number of articles (Izashvili, 1940; Gvazava, 1957; Khuskivadze, 1954; Vartapetov, 1947, 1957). More recent studies (Shvelidze, 1970) were performed on a group of 161 patients with chronic and frequently relapsing infections with the following diagnosis: 62 patients with furuncles (boils) and furunculosis, 57 with carbuncles and 45 with hydroadenitis. In all cases antibiotic therapy with penicillin, biomicon, streptomycin had been performed without a positive outcome.

Duration of the chronic diseases varied from 2-3 months to 15-20 years. All the patients claimed to have high temperatures (37- 37.8^{O}C), headaches, weakness, insomia and movement difficulties. Most of the patients with furuncles had 1-12 boils in different parts of the body. Microbial analysis of specimens obtained from the 161 patients identified 139 strains of coagulase-positive Staphylococcus. The 83% of these strains appeared to be penicillin-resistant. Phages were administered topically as applications and injected subcutaneously around the infected locus. In total 95 % (152 cases) were completely cured, 4.3% (7 patients) showed significant improvement and in 1.3% (2 patients) the treatment had no effect. Long-term surveillance was performed over the next 4 years. Relapse was observed after 3-6 months in 8,5 % of cases only. These patients underwent an additional course of the phage therapy after which they were completely cured. The results are summarized in Table 1.

Table 1: Effect of phage therapy for treatment of certain forms of dermal infections caused by *Staphylococcus aureus*

Groups	Diagnosis	Number of patients	Type of therapy	Duration of treatment (min-max)	Complete cure (%)	Improvement (%)	Temporary effect (%)	No effect (%)	Re-infection (%)
Exp. Gr 1	Furuncu-losis	62	Phage	3-10 days	97.7	3.3	-	0	4.8
Control 1	Furuncu-losis	62	Anti-biotics	3 months 16 years	0	53.3	20.9	25.8	100
Exp. Gr 2	Carbun cu-losis	54	Phage	5-10 days	66.7	20.0	-	13.3	11.1
Control 2	Carbun cu-losis	54	Anti-biotics	2 months 15 years	0	7.4	92.6	0	100

The control groups are presented by the same groups of patients previously treated with antibiotics (Shvelidze, 1970).

Combined phage and antibiotic therapy

The end of the 1950s and beginning of the 1960s was marked by the emergence of a new direction in Soviet medicine. The researchers started to elaborate regimens by combining phages and antibiotic therapies (Jakobson, 1956; Sheviakova et al, 1956: 1958: 1961; 1964). From these types of experiment, the work accomplished by Vepkhvadze (1974) is especially remarkable. She carried out *in vivo* studies on a mouse model. The 20 mice in each group were infected with antibiotic resistant *Staphylococcus aureus.* The groups were then treated with the specific *Staphylococcus* phage (a product of the IBMV, Tbilisi, Georgia) alone, with the antibiotics alone and the phages in combination with different antibiotics (dichlortetracycline, erythromycin, pasomycin, oxacylin). In the first series of experiments the antibiotics and the phages were administered immediately after infection. In the second series, the phages were administered immediately after infection, while the antibiotics were added with different intervals of time (4, 8, 24 hours after infection). In the third series, the antibiotics were administered immediately after infection, while the phages were given 4-8-24 h. after this. It was shown that results of treatment performed separately with either sub-therapeutic doses of phages (app. titre 1 x 10^7 pfu/ml) or antibiotics (3200 μg/ml), are quite similar (Table 2). However, for the combined use of antibiotics and phages, the best results were achieved when the antibiotics were administered 24 hours prior to phage treatment. It was recommended to use the bacteriophages in combination with the antibiotics but with the shift of 24 hours. The data presented in Table 2, shows the greater efficacy when phage were administered 24 hours after administration of antibiotic and microbial challenge with 75% of mice surviving to day 15^{th}.

From 40% to 65% of mice survived, correspondingly, in the cases of the 4 and

8 hours delayed administration of phages. The control groups, where only erythromycin was administered simultaneously with the challenge indicated 45% of survival and, in the group where only phage was administered after 24 hours the survival rate was 35% (Vepkhvadze, 1974).

Table 2: Combined application of the phages and antibiotics

Preparations	Administration	Number of mice	Number of survived mice through the 15th day		P	Average life expectancy (days after manipulation)
			Abs. Number	%		
Phage + Ery	Simultaneously with infection after 4 hours	20	8	40	> 0.5	6.7
Ery alone	After 4 hours	20	10	50	>0.5	7.7
Phage + Ery	Simultaneously with infection after 8 hours	20	7	35	> 0.5	5.6
Ery alone	After 8 hours	20	9	45	>0.5	6.6
Phage + Ery	Simultaneously with infection after 24 hours	20	8	40	-	5.8
Ery alone	after 24 hours	20	8	40	-	6.6
Ery + Phage	Simultaneously with infection after 4 hours	20	8	40	-	6.4
Ery alone	Simultaneously with infection	20	9	45	>0.5	7.3
Phage alone	4 hours after infection	20	8	40	-	3.2
Ery + Phage	Simultaneously with infection after 8 hours	20	13	65	-	8.1
Ery alone	Simultaneously with infection	20	9	45	>0.2	7.3
Phage alone	8 hours after infection	20	7	35	< 0.05	3.6
Ery + Phage	Simultaneously with infection after 24 hours	20	15	75	-	9
Ery alone	Simultaneously with infection	20	9	45	<0.05	7.3
Phage alone	24 hours after infection	20	7	35	<0.01	2.4

The table is borrowed from the Ph.D.dissertation of Dr. L.Vepkhvaadze.

S. aureus phage for intravenous use

Although the trails of intravenously administration of phages started at the very early stages of clinical experiments in 1930s and 1940s, this type of therapy was rejected due to the unfavorable side effects including rising temperature, up to 38-39°C, shivering, headaches, etc. However, a lethal outcome has never been reported (Tsulukidze, 1938; Ukelis, 1940). The highest and the most recent achievement among the activities of the Eliava Institute of Bacteriophage is elaboration of the apyrogenic *Staphylococcus* phage for intra-venous use (Chirakadze, Chanishvili, 1964; Chanishvili T., *et*

al., 1974; Nadiradze M.M, 1984), the action of which was proved in clinical experiments on adults and children. Altogether 900 patients were involved in this study, among them 247 children aged between 1 day and 15 years and 653 adults in the aged 15-72. The 494 persons were treated with phages alone or in combination with antibiotics and/or immune-stimulating means. The 406 persons from the control group were treated with antibiotics only. Intravenous use of phages did not have any significant side effect.

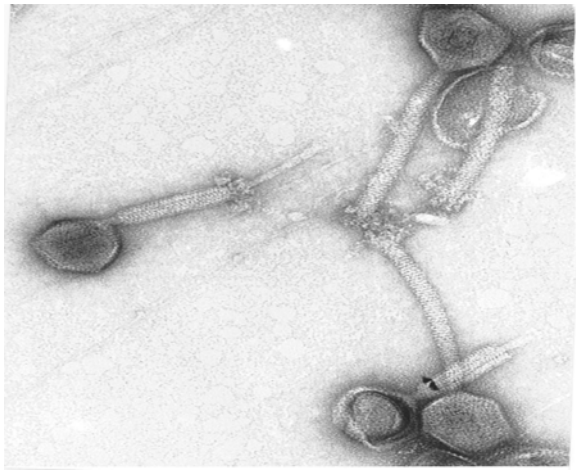

Figure 4. The phage Sb-1 related to *S. aureus* used as a component of the intravenous bacteriophage preparation.

After this experiment the Staphylococcus phage was produced by the industrial part of the Eliava Bacteriophage Institute and successfully applied in many clinics throughout the whole territory of the former Soviet Union (Fig. 4). The phage was applied for intra-venous use in infusions, transfusions and injections. It was mostly used for treatment of the chronic septicaemia, for treatment and prophylactics of eye, ear, throat, lung diseases, for healing burned wounds, bacterial consequence of surgical operations on bones and skull, women infertility related with bacterial inflammation problems and so on (Chkhetia, 1984; Samsygina, 1985; Bochorishvili, 1988).

Table 3: Effect of phage therapy in the cases of septicaemia among adults and children

	Adults			**Children**		
	Number of cases	Fatal cases	Per cent of mortality	Number of cases	Fatal cases	Per cent of mortality
Experimental Group	215	0	0	149	1	0.67
Control Group	308	11	3.6	98	8.2	
Total	653	11	1.68	247	9	3.6

Prophylaxis

In the former Soviet Union the phages have been extensively used for prophylaxis as well, especially for communities where the spread of infections might be rapid such as kindergartens, schools, military accommodation etc. According to the review written by Krestovnikova, (1947) an experiment on prophylactic use of phages was successfully accomplished in 1935 on thousands of people in the regions with high incidence of dysentery. Later on different modifications of the dysenterial phages, namely dry tablet forms have been included into the clinical studies. One of the latest studies describes the results of preventive treatment performed with the phage tablet forms having an acid-resistant coverage (Anpilov, Proskudin, 1984). Experimental and control groups were formed according to accidental selection, one soldier was taken as an observation unit. The persons in the experimental and control groups, that were located in different geographical zones of the USSR, however were placed in the similar epidemic conditions. The coded bacteriophage preparations and placebo were given seasonally during the rise of morbidity (threat of epidemics), in particular in June-July and in September-October. The coded preparations were given to the persons from experimental and control groups 1.5 - 2 hours prior to meals, 2 tablets each time. One group of people was receiving these tablets at intervals of 3 days, while another group was receiving them at 5 day intervals. Calcium gluconate was used in placebo experiments. The phage and placebo was given to every second person, thus providing quantity and quality equity of the experimental and control groups. Efficiency of prevention of the phage prophylactics taken once per 3 days was 75%, and 67% when taken once per 5 days. Thus, a conclusion was drawn according to which it was recommended to use the phage tablets once per 3 days.

Phages versus antibiotics

One of the areas that have made the idea of phage therapy attractive once again is the increasing prevalence of antibiotic resistant bacteria. The widespread use of antibiotics in modern medical practice is related to their rapid antibacterial action and broad spectrum of activity. This last characteristic is crucial in the treatment of diseases where the pathogens have not been identified but therapy is required immediately. However, antibiotic usage has negative effects some of which are becoming increasingly important including, generalized, non-specific antimicrobial activity that damages the normal microflora enabling colonization by opportunistic pathogens.

- Side effects, such as allergy and toxicity, including effects on the immune system.
- Selection of antibiotic-resistant bacteria and enhanced rates of transfer in the absence of the normal flora
- Enhanced spread of fungal and yeast infections.

Phage therapy/prophylaxis has a number of attractive advantages:

- Bacteriophages are highly specific for the target bacteria without affecting the normal microflora and are effective against multiple drug-resistant bacteria.
- Following numerous studies in animals and from clinical experience no adverse side effects have been observed. Purified phage preparations do not cause significant side effects such as allergy, intoxication, etc.
- Because of their ability to multiply in the target hosts a single dose treatment can be envisaged for many diseases.
- The environment provides an almost inexhaustible source of new active phages when required. Ecological safety of phages is implied by their high specificity towards the target bacteria. Bacteriophages will therefore not accumulate in the environment.
- Production of bacteriophages is economical. It does not require sophisticated and expensive equipment or complicated and multi-stage technologies.

SUMMARY

In summary, despite the early failures in the West, countries in the former Soviet Union have continued to use bacteriophages for disease therapy and prophylaxis and sterilization purposes with apparent success. Given the increasing concern over multiple antibiotic resistance in a number of bacterial pathogens, this is an area of disease control whose potential is proven and should be reviewed.

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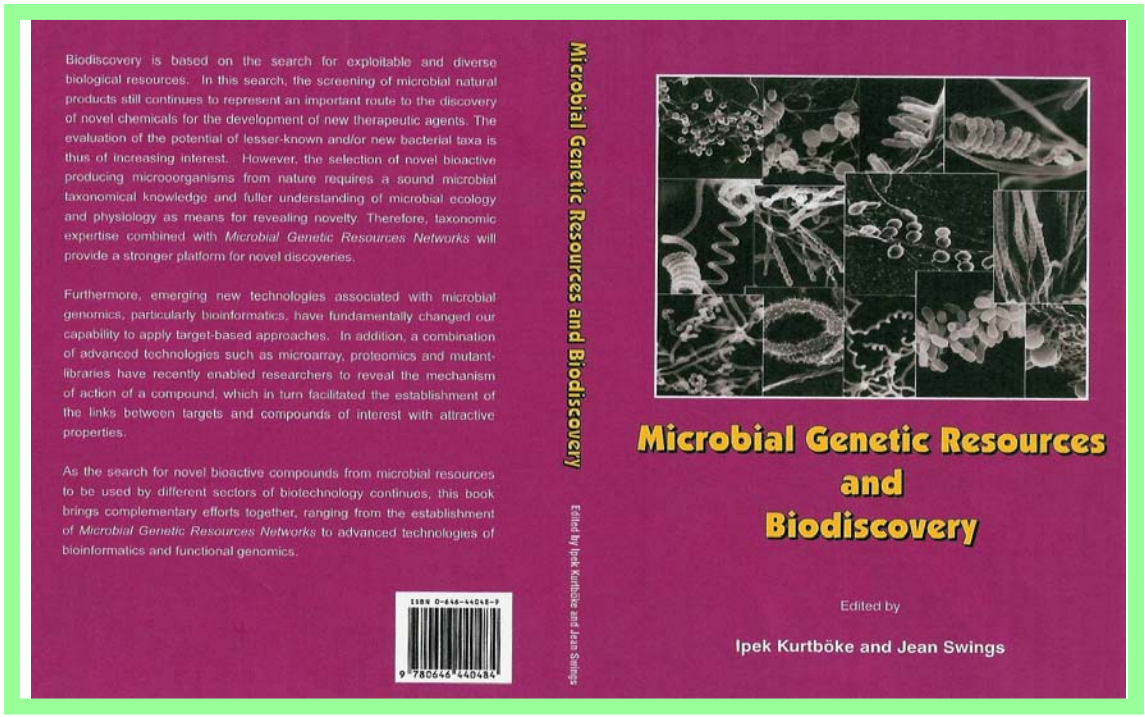

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