# Biological Resource Centres

## UNDERPINNING THE FUTURE OF LIFE SCIENCES AND BIOTECHNOLOGY

SCIENCE AND TECHNOLOGY


OECD

# BIOLOGICAL RESOURCE CENTRES

## UNDERPINNING THE FUTURE OF LIFE SCIENCES AND BIOTECHNOLOGY


ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT

# FOREWORD

*Biological Resource Centres: Underpinning the Future of Life Sciences and Biotechnology* appears 19 years after the OECD's first report on biotechnology (*Biotechnology – International Trends and Perspectives*, 1982) when experts and policy circles were still wondering whether this new technology was just one new tool in the changing toolkit of the chemicals industry, or whether it had perhaps more far-reaching significance.

*Biological Resource Centres* appears at the beginning of what has been called the "century of the life sciences" and in a radically different intellectual environment. The turn-about in political and public perception began in 1999-2000, triggered by the crisis over genetically modified food in Europe and the sequencing of the human genome.

There is now little doubt that the breakthroughs in biotechnology, genomics and genetics will affect our societies and many aspects of our life as profoundly as information technologies have already done. However, there is still only scanty awareness that biotechnology will lead to many changes in government policy, public information, law, education and the scientific and technological infrastructure.

This report alerts policy makers and the public to the fact that the framework conditions of the new technology, its scientific and technological infrastructure and its raw materials differ greatly from those that underpinned earlier technologies. Understanding of these differences will be essential if the technology is to develop successfully. How do we move from technologies based on mineral resources (metals, coal, oil, etc.) and on physics, chemistry and engineering to technologies increasingly based on biological resources and, more particularly, on something that is essentially invisible – the living cell and its genes?

In 1998, Japan had the foresight to propose that the OECD's Working Party on Biotechnology should examine support for Biological Resource Centres – BRCs – as a key component of the scientific and technological infrastructure of the life sciences and biotechnology. This effort began with the

"OECD Workshop Tokyo '99 on Scientific and Technological Infrastructure – Support for BRCs", which was held in Tokyo on 17-18 February 1999.

This report is the result of two years of work by a Task Force on Biological Resource Centres. While at the outset, opinions of representatives of different countries and disciplines varied widely, they ultimately converged on all substantive issues. Thanks are due to all participants (see Annex 3), but particularly to the Task Force chairs and consultants who represent a wide spectrum of international competence. They include the chair: Prof. Hideaki Sugawara, Director of WFCC-MIRCEN World Data Centre for Microorganisms and Head of the Database Management and Development Division of DNA Data Bank of Japan; the vice-chairs: Prof. Ross Coppel, Head of the Department of Microbiology, Monash University, Australia; Prof. Jay Grimes, Dean of Marine Sciences, University of Southern Mississippi, United States; and Prof. Erko Stackebrandt, Director of the German Collection of Microorganisms and Cell Cultures, Braunschweig. Key contributors are: Prof. Ron Atlas, Dean of Graduate Studies, University of Louisville and President Elect of the American Society of Microbiology who developed the architecture of the report; Prof. Mark Bailey, Institute of Virology and Environmental Microbiology, Oxford; Dr. Alan Doyle, Biological Collections Programme Manager, Wellcome Trust, London; Prof. Toru Okuda, Tamagawa University, Tokyo; Mr. Louis Réchaussat, Director of the Information System Department of the National Institute of Health and Medical Research (INSERM), Paris; Ms. Andrée Sontot, Bureau of Genetic Resources, Paris; and Dr. Seizo Sumida, Managing Director, Japan Bioindustry Association.

The OECD Secretariat participated in the common effort through the undersigned and his colleague, Dr. Yoshiyasu Yabusaki.

The Task Force and the Working Party on Biotechnology are issuing a "Call for Action by OECD Countries and Beyond" (Chapter 7), which consists of five recommendations. The last of these calls for the establishment of a Global BRC Network. France agreed in March 2001 to take over from Japan the lead role and to pilot the BRC follow-up activity. This new phase will prepare for the implementation of the recommendations: the stakes are high, but so are the rewards.

Dr. Salomon Wald
Head of the Biotechnology Unit (January 1999 to May 2001)
OECD Directorate for Science, Technology and Industry

Paris, March 2001

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## EXECUTIVE SUMMARY

**"***Biological resource centres are an essential part of the infrastructure underpinning life sciences and biotechnology. They consist of service providers and repositories of the living cells, genomes of organism, and information relating to heredity and the functions of biological systems. BRCs contain collections of culturable organisms (*e.g. *micro-organisms, plant, animal and human cells), replicable parts of these (*e.g. *genomes, plasmids, viruses, cDNAs), viable but not yet culturable organisms, cells and tissues, as well as databases containing molecular, physiological and structural information relevant to these collections and related bioinformatics.*" (Definition based on the one adopted at the 1999 Tokyo Workshop on Biological Resource Centres, where the concept of BRCs as an outgrowth of conventional pre-genomics ex situ collections of biological materials was developed – and incorporating scientific developments since 1999.) *BRCs must meet the high standards of quality and expertise demanded by the international community of scientists and industry for the delivery of biological information and materials. They must provide access to biological resources on which R&D in the life sciences and the advancement of biotechnology depends.*

Biological resource centres are essential for R&D in the life sciences, for advances in the quality of the environment, agriculture, and human health, and for the commercial development of biotechnology. Their many crucial roles include:

- Preservation and provision of biological resources for scientific, industrial, agricultural, environmental and medical R&D and applications.
- Performance of R&D on these biological resources.
- Conservation of biodiversity.
- Repositories of biological resources for protection of intellectual property.
- Resources for public information and policy formulation.

The Convention on Biological Diversity (CBD), which was adopted in 1992, highlighted the need for comprehensive scientific study of biological diversity and raised the importance of BRCs in the eyes of governments and the scientific community. Vast numbers of organisms distributed around the globe will be studied and become biological resources for the life sciences and biotechnology. Just three years after the Earth Summit of 1992, the entire sequence of the genome of the bacterium *Haemophilus influenzae* was completed, and, for the first time, the full set of genetic information of a living organism was known. Genome sequencing has accelerated since then; every month on average, an additional microbial genome is made available. We now see numerous living organisms as resources, with millions of genes and molecules available for the life sciences and biotechnology. New discoveries are made daily that challenge BRCs. The new century will see an explosion in the availability of heterogeneous biological materials which will make the role of BRCs even more critical.

Biodiversity and genomics will be the source not only of tremendous amounts of biological materials, from large organisms to miniature genes, but also of a "tsunami" ("tidal wave") of data that will be a key to R&D in the life sciences. In the 21st century, biology will be studied increasingly *in silico* (computationally) in order to extract information and knowledge from this wealth of data.

Biological materials and data have long been preserved in and disseminated by repositories of microbial culture collections, seed banks, etc. These biological collections face great challenges but also great opportunities owing to the explosive increase in biological materials and data. It is against this background that the OECD's Working Party for Biotechnology endorsed Japan's proposal to examine support for BRCs, which are now seen as repositories of a new kind, and as a key element of the scientific and technological infrastructure.

It is increasingly difficult for governments to supply the full financial support necessary to ensure the sustainability of BRCs so that they can perform essential functions for scientific R&D, health, and biotechnology. Maintaining and enhancing quality are essential but difficult to achieve in the face of increasing demands for services. To be effective engines for the advancement of the life sciences and biotechnology, BRCs must provide access to the wealth of biodiversity and information on genomics. However, a variety of factors tend to restrict access. Many are legitimate, but if they are the consequence of a lack of international harmonisation, they can be alleviated.

In order to secure this essential infrastructure, national governments should undertake the following actions in concert with the international scientific community:

- Selectively seek to strengthen existing *ex situ* collections of biological data and materials, create collections of new resources, including in non-OECD countries, and elevate those collections to the quality required for accreditation as national BRCs.
- Support the development of an accreditation system for BRCs based upon scientifically acceptable objective international criteria for quality, expertise and financial stability.
- Facilitate international co-ordination among national BRCs by creating an agreed system of linkage. This should be based upon modern informatics systems that link biological data to biological materials across national BRCs and upon common technological frameworks.
- Take into account the objectives and functioning of BRCs when establishing and harmonising national or international rules and regulations.
- Develop policies to harmonise the operational parameters under which BRCs function, including those governing access to biological resources as well as their exchange and distribution, taking into account relevant national and international laws and agreements.
- Support the establishment of a global BRC network that would enhance access to BRCs and foster international co-operation and economic development.

## *Chapter 1*

# THE NEED FOR BIOLOGICAL RESOURCE CENTRES

Biological resources – living organisms, cells, genes, and the related information – are the essential raw materials for the advancement of biotechnology, human health, and research and development in the life sciences. The revolution in molecular biology has given us greatly increased ability to obtain and to modify these biological resources and to use them for the benefit of all humankind. The sequencing and the associated analysis of gene functions for a growing number of genomes will have an unprecedented effect on the uses of biological resources and the need for access to them. Governments and industry are making large investments in recovering biological resources from nature and in exploring and engineering these resources. Their efforts include the human genome. These investments must not be lost and their results must remain accessible so as to reap scientific, economic and medical benefits.

## Defining biological resource centres

Access to biological resources will require repositories and distribution nodes, collectively called biological resource centres (BRCs), which will be responsible for preserving and distributing biological materials and information.

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*quality and expertise demanded by the international community of scientists and industry for the delivery of biological information and materials. They must provide access to biological resources on which R&D in the life sciences and the advancement of biotechnology depends.*

The growing worldwide demand for biological resources provides good reasons for greatly increasing the number and quality of BRCs. Only a very few large national centres are able currently to perform a comprehensive role and to provide access to diverse organisms, such as bacterial, fungal, plant and animal cells, including human genes and cells. (See Box 1.1 for a description of one of these multifunctional centres.) Other centres play much narrower, yet important, roles, supplying limited but crucial specialised resources. The development, expansion and survival of these BRCs face many challenges. These include those posed by the molecular revolution (genomics and the information revealed by DNA sequencing), accelerating efforts to conserve biodiversity, funding uncertainties that threaten stability, the need for adequate quality assurance and constraints on access to biological resources within countries and across international borders resulting from private industry's protection of investments and industrial secrecy, import/export regulations, intellectual property rights, safety issues and ethical concerns about the uses of genes and other biological resources.

This report identifies the policy, organisational and economic challenges faced by BRCs and makes recommendations to governments for national and international solutions.

## Functions of biological resource centres

Why are BRCs needed? What are their essential functions? Why should governments and the private sector care about them and take steps to ensure their survival? Why are the current repositories of biological resources, including *ex situ* culture collections of micro-organisms and other living cells, housed in many countries in institutions that are often not connected to each other and are inadequate to meet the world's needs for biological resources?

The answers to these questions lie in the many roles played by BRCs:

- Preservation and provision of biological resources for scientific, industrial, agricultural, environmental and medical R&D and applications.

- Performance of R&D on these biological resources.
- Conservation of biodiversity.
- Repositories of biological resources for protection of intellectual property.
- Resources for public information and policy formulation.

### Preservation and provision of biological resources for scientific, industrial, agricultural, environmental and medical R&D and applications

By making available biological materials and information of guaranteed identity and quality, BRCs serve an essential infrastructural function for scientific investigation and R&D. Scientific enquiry requires reproducibility: experiments performed in one laboratory by one set of investigators must be replicable in another laboratory. The reliability of biological resources is as important as the purity of chemical reagents and the precision of equipment used to conduct scientific research. The availability of known, validated and precisely identified biological resources is essential for research.

BRCs are also essential sources of information and materials for industrial and many other practical uses. Given that enormous sums are invested in extracting organisms and their genes from nature and elucidating the genetic and functional molecular elements of those living resources, it is essential for these biological resources not only to be preserved but also to be used. BRCs provide the genetic elements, organisms and information used in biotechnological, agricultural, environmental and medical applications. Without them, every user would have to "reinvent the wheel" and invest innumerable hours in the costly recovery of organisms and genes and their characterisation.

### Performance of R&D on these biological resources

BRCs have opportunities to carry out R&D on the biological resources they house. They often have the expertise needed to further the identification, characterisation and preservation of biological resources. Their R&D activities can contribute to the advancement of the life sciences and may result in valuable products that can help generate income to support the BRCs' broader functions. However, BRCs must balance this R&D function with their service function, providing and preserving biological resources for the wider scientific, industrial, agro-food and medical communities.

## Conservation of biodiversity

Microbial culture collections, viral repositories, herbaria, botanical gardens, zoos and *ex situ* plant and animal genetic resource collections all help preserve biodiversity, which is threatened by unsustainable economic development, natural disasters and global change. The benefits of the conservation of biological resources are emphasised by the Convention on Biological Diversity (CBD), which highlights the need for BRCs as *ex situ* conservatories of biodiversity. Under the terms of the CBD, biological resources include genetic resources, organisms or parts thereof, populations or any other biotic component of ecosystems with actual or potential value for humanity. A number of factors link the CBD to BRCs as conservatories of biodiversity, including:

- The intrinsic ecological, genetic, social, economic, scientific, educational, cultural, recreational and aesthetic values of biological diversity and its components.
- The importance of biological diversity for evolution and the life-sustaining systems of the biosphere.
- The conservation and sustainable use of biological diversity for meeting the crucial food, health and other needs of the growing world population, which requires access to and sharing of both genetic resources and technologies.

## Repositories of biological resources for protection of intellectual property

Several collections, called International Depository Authorities (IDAs) in the Budapest Treaty (Budapest Treaty on the International Recognition of the Deposit of Micro-organisms for the Purposes of Patent Procedures), serve as legally mandated repositories of biological resources for the purpose of implementing IPR agreements. For micro-organisms, other cells and genetic elements, these are defined by the Budapest Treaty; for plant varieties, a service is defined by the International Union for the Protection of New Varieties of Plants (UPOV) treaty; such deposits are also defined in the EU Directive on the protection of biotechnological inventions. Since 1981, the Budapest Treaty has harmonised deposition procedures and patent applications. In accordance with the Budapest Treaty, IDAs maintain secrecy about the deposited resources but must furnish samples of deposited micro-organisms to entitled third parties on application to the national patent authorities.

Some culture collections also provide a special service for long-term preservation of micro-organisms whose distribution may be restricted at the discretion of the depositor. Such "safe deposits" of biological resources are a way to ensure long-term preservation without loss of ownership. This method does not comply with the requirements of a patent deposit but provides the equivalent of the protection of a "trade secret".

## Resources for public information and policy formulation

BRCs provide essential expertise for formulation of government policies on biological resources and for information and assurance to the public. They can thus serve as an important interface between government, industry and the public and can help the public understand the value of conserving biological resources. They are bodies which the public and policy makers can call upon for objective help in developing regulations and guidelines for the safe and ethical use of biological resources, including those derived from human genes. Countries' laws and regulations governing access to biological resources and their exchange differ and international efforts for harmonisation (see Annex 2) should increase. Ethical issues (especially for human genetic material and the need for confidentiality and prior informed consent) are increasingly crucial public issues which policy makers must address. Much assistance from BRCs will be needed to develop and implement policies on the uses of biological resources in the age of molecular biology heralded by the genomics revolution.

Box 1.1. **The Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (German Collection of Micro-organisms and Cell Cultures) (DSMZ): A comprehensive centre with multiple functions**

The DSMZ is an independent service and research organisation dedicated to the acquisition, characterisation and identification, preservation and distribution of bacteria, archaea, fungi, yeasts, plasmids, phages, human and animal cell lines, plant cell cultures and plant viruses. It is a non-profit, scientific institution and a centre of national importance located in Braunschweig. It is financed by the federal government (40%), the federal states (40%) and income (20%).

The DSMZ is the most comprehensive resource centre of micro-organisms, cell lines and plant viruses in Europe. As the national depository of patented biological material of this kind, it is an IDA (International Depository Authority) as defined in the Budapest Treaty and offers industry and academic research authentic, state-of-the-art preserved biological material. Its functions include:

- Collection and maintenance of the biological diversity of micro-organisms, cell lines and plant viruses.
- Worldwide shipment of cultures.
- Research relevant to the needs of the collections and on issues of biodiversity and ecology.
- Identification, characterisation and certification, including molecular approaches.
- Patent and safe deposits.
- Databases, catalogues and brochures covering each of the collections in electronic and printed format.
- Individual training.

The DSMZ currently has a collection of more than 8 700 strains of bacteria and archaea of almost all described species, 100 bacteriophages, 2 300 filamentous fungi, 500 yeasts, 740 plant cell cultures, 700 plant viruses and 400 human and animal cell lines, which is accessible to the scientific community. The breadth and depth of its collections of archaea and extremophiles (organisms growing under the most extreme conditions where life can exist, the conditions which also characterise many industrial processes where biotechnology may be applied) make it a unique biological resource.

The DSMZ culture collections and scientific services are used not only in basic research but also for elucidating and solving environmental problems, for industrial production processes and for ecological development.

*Chapter 2*

# THE INCREASING CHALLENGES OF BIODIVERSITY AND GENOMICS

Worldwide attempts to preserve biodiversity and the information and materials generated by the genomics revolution present a significant new challenge to governments and industry. What biological resources should be preserved? Where should they be preserved? Who should be responsible for their preservation? How can governments co-operate to enhance efficiency? How can *ex situ* collections of biological resources cope with the wealth of biodiversity and the vast quantity of information and products emerging from the genomics revolution? There is currently no binding governmental or scientific guidance, nationally or internationally, to avoid unnecessary duplication of effort in acquiring and maintaining biological resources (some duplication however, is justified and warranted). As a result, governments and industry have, for the most part, developed separate strategies that now are in need of co-ordination. BRCs are operating without guidance on how to deal with the growing influx of biological materials and data that should be preserved and made accessible. BRCs and governments jointly face the daunting challenges of biodiversity and genomics.

## Challenge of biodiversity

Important efforts are underway to maintain plant and animal biodiversity under *in situ* conditions (*e.g.* within ecological reserves, natural habitats, on farms) and in *ex situ* collections (*e.g.* within zoos and botanical gardens), and efforts for the rationalisation of conservation are already under way at national and international levels (see Box 6.5). The situation is more difficult for the extensive but invisible microbial world, given that less than 1% of microbial biodiversity has been identified, and that microbial biodiversity is best preserved *ex situ*. The challenge faced by existing collections and future BRCs is enormous: should they aim at the conservation of all biological diversity? How are BRCs to cope with the vast influx of new biological resources, especially in the microbial domain? How can they possibly link all relevant information to so diverse a group of organisms?

## *Biological Resource Centres*

All countries are experiencing difficulties in interpreting and implementing the CBD. Communication among research facilities concerning the specification of the genetic identity of organisms will be needed to ensure transparency of lineage for such organisms. This communication will be a prerequisite for the appropriate exploitation of biological resources. Countries may find BRCs a unique mechanism for coping with the demands of the CBD, especially if they are joined in a co-ordinated system of BRCs but still preserve the national sovereignty of their biological resources. (Box 2.1 describes a new centre for the conservation of global plant biodiversity.)

Box 2.1. **The Millennium Seed Bank: Conserving plant biodiversity**

The Millennium Seed Bank Project at the Royal Botanic Gardens in Kew, near London, opened on 26 August 2000. The Wellcome Trust provided nearly USD 14 million for a building constructed to house seed vaults, and a USD 45 million grant from the National Lottery for this project is being used to support a world resource for seed conservation, research and education.

This project establishes a new standard of quality for seed banks and has two principal aims: *i)* collection and conservation by 2010 of 10%, over 24 000 species, of the world's seed-bearing flora; and *ii)* collection and conservation of seeds of the United Kingdom's entire native seed-bearing flora before 2001. Other goals of the project are to: *i)* carry out research to improve all aspects of seed conservation; *ii)* make seeds available for research and species reintroduction into the wild; *iii)* encourage plant conservation throughout the world by facilitating access to and transfer of seed conservation technology; *iv)* maintain and promote public interest in plant conservation; and *v)* provide a world-class facility as a focal point for this activity.

One of the most important aspects of the Millennium Seed Bank Project will be to share expertise in seed conservation with collaborating countries. Ultimately, the project aims to assist other countries to set up their own seed bank resource centres. The Millennium Seed Bank Project aims to better the understanding of the underlying processes of seed traits, such as germination and storability, thus improving the efficiency of seed-banking methods. Low-technology solutions to seed conservation problems are being sought and the intent is to achieve technology transfer and capacity-building through formal and informal training.

The Millennium Seed Bank is a global resource centre; as such, it will make seeds available to researchers, conservationists and scientific institutions throughout the world free of charge, guided by the terms and conditions of the Convention on Biological Diversity.

A major role of BRCs, in the final analysis, is to take a living object as it might be found in nature and to name and describe it, in other words to make it into a "product" that is the starting point of any collaborative research and technology transfer. BRCs that operate on the basis of scientific and technical criteria acceptable to the world scientific community offer the *de facto*

guarantee of accessibility and transparency required by the CBD. This should alleviate distortions in the implementation and interpretation of the CBD and provide a basis for the facilitation of international exchange of biological materials.

## Challenge of genomics and functional genomics

BRCs must 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 genomes. 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 for BRCs.

Genomics and functional genomic studies are generating extraordinary amounts of information and taxing the capabilities of informatics for analysing and using data. Biologists and biotechnologists will spend the next few decades understanding and exploiting the information provided by these genome-sequencing efforts. These sequence data and their by-products – *e.g.* genome libraries, expression microarrays and protein chips – have to be preserved and made easily accessible. The quest to obtain information on each of the thousands of genes, gene products and other characteristics of each organism highlights the daunting task faced by BRC data banks in storing, maintaining, disseminating and cross-referencing this information. Similarly, many products of genetic modification – ranging from genetically engineered bacteria to transgenic plants and animals – must be preserved for scientific investigations and for commercial applications of biotechnology, as well as for regulatory and safety purposes (Box 2.2 describes a centre focusing on mouse genomics).

Box 2.2. **The Jackson Laboratory: A leader in the genomics revolution specialising in mouse models**

The Jackson Laboratory at Bar Harbor, Maine, in the United States is an independent non-profit mammalian research laboratory funded by grants from the federal government and others and by the sale of products derived from research. Jackson Laboratory extracts, purifies, preserves and distributes high quality DNA from mice, providing molecular biologists with a source of DNA that has been subject to rigorous quality controls which ensure the standardisation, health and genetic purity required for scientific research. The laboratory operates the world's largest frozen mouse embryo repository. It preserves important stocks and strains of mice for use in research. The Mouse Mutant Resource is unique in its ability to identify new mutations and complex breeding patterns that allow reproduction and maintenance of new mutant mouse stock lines.

The Jackson Laboratory is an invaluable resource for genetic information because of a computerised database system which can be accessed from anywhere in the world and gives fast, efficient access to a single comprehensive archive on basic research's most widely studied animal – the mouse. The Jackson Laboratory offers a transgenic mouse resource that makes it possible to insert human genes, for example, into mouse embryos. This means that scientists have access to an *in vivo* test system for studying functions of human genes. The most powerful approach to determining the bases of human diseases, including cancer, is identification and functional analysis of genes in model organisms. The bioinformatics databases at the Jackson Laboratory provide the resources needed by the international scientific community to explore the genetic control of function and dysfunction in mice and humans.

The Jackson Laboratory's importance as a resource centre for genetically defined mice was clearly demonstrated by the impact of a 1989 fire that destroyed portions of the facility and nearly 400 000 mice. Many cancer and other research projects in the United States, Europe, and Japan were delayed for months while the laboratory replenished it stocks of "JAX" mice, which are the world's genetic "gold standard" for mice.

## Meeting the challenges

To cope with the massive expansion of biological resources, including living biological materials and data on genomics, BRCs need to:

- *Contribute to the co-ordination of efforts to conserve biodiversity and to provide access to natural and engineered biological resources.*
- *Assist in the development of a co-ordinated international system for decision making to guide appropriate acquisition, maintenance and distribution of biological resources so as to avoid unnecessary duplication of effort while preserving critical levels of biodiversity.*

- *Modernise to incorporate the latest developments in Web-based electronic communication, bioinformational science and informatics technologies.*
- *Co-ordinate and unify catalogues and databases to meet the requirements of science in the developing post-genomics era.*
- *Develop new systems and technologies for the long-term maintenance and distribution of large numbers of diverse biological resources.*
- *Play an active role in the development of new technologies for culturing and preserving the not yet culturable micro-organisms.*
- *Co-ordinate curation, as well as development and networking of informatics tools for data analysis, comparison and visualisation.*
- *Ensure that the scientific community has access to affordable products and services.*

*Chapter 3*

# FINANCIAL SUPPORT FOR LONG-TERM STABILITY

The long-term stability of BRCs requires adequate and reliable sources of funding. But how much core support must come from governments? How can other sectors contribute to the functioning of BRCs? What models of funding or partnerships can be used to ensure the sustainability of BRCs? What constitutes an adequate support base for the sustainability of a national BRC? Can costs be lowered through international co-operation? Is there a threat that some valuable biological resources will be lost to the global community owing to lack of funding? Many biological resources that have been maintained by single individuals, institutions or companies are at risk of becoming "orphan collections" and appear to face uncertain futures. High-quality BRCs that meet the needs of industry and the scientific community require long-term guaranteed financial support to maintain their mission and infrastructure. A serious problem will arise if BRCs reach an agreement to form a network aimed at eliminating duplication and sharing biological resources should one of the members or nodes in that network fail for lack of support. (Box 3.1 describes the case of an orphan collection that was saved by a foreign country.) Furthermore, as an important part of the richness of biodiversity is deposited in BRCs, the need for new and creative sources of funding will become more critical. The promise of biotechnology is inextricably linked to appropriate support of BRCs.

## Financial costs of BRCs

The cost of incorporating biological resources into BRCs has escalated, limiting the functioning of BRCs. The DSMZ (see Box 1.1) estimates that it costs USD 2 500-3 000 to add a bacterial culture to its collection. Given that an estimated three million bacteria remain to be isolated from nature, their acquisition and incorporation into BRCs would cost USD 9 billion. The American Type Culture Collection (ATCC) estimates that it costs between USD 5 000 and USD 10 000 (depending on the type and quality of the material – tissue cultures, organisms, databases, etc.) to add new items to its collection when the costs of quality control, validation, long-term preservation and global distribution are taken into consideration. Funding such huge costs and ensuring

continuous support for maintenance and functioning of BRCs will require creative international financing arrangements.

Box 3.1. **Japanese rescue of an orphan American collection of medical bacteria**

What happens to organisms and data that have been collected by individuals when those individuals retire or die? Should the bioresources, which may have been exchanged with the wider scientific community and which may be crucial to future R&D across international borders, also disappear or perish? Or should the bioresources be transferred to a BRC? If so, to which BRC should they go and how should the transfer be supported? These questions apply to many microbial culture collections at universities and in industry which have become "orphan collections" owing to the loss of the individual responsible for overseeing and championing the collection.

To illustrate the dilemma, consider the fate of the valuable collection of medically relevant bacteria established by Dr. Rudolph Hugh at George Washington University in the United States. Cultures from the collection were being supplied to Japan and other countries for biomedical R&D. When Dr. Hugh retired, the collection was going to be destroyed, with a significant loss of biological resources for the international scientific community. Experts on medical bacteria were alarmed, and Japanese scientists arranged to transfer about 3 500 strains of *Pseudomonas*, *Vibrio* and *Aeromonas* to the Japan Collection of Microorganisms (JCM). JCM, which supplies authentic micro-organisms to researchers in the fields of life sciences and biotechnology, is part of RIKEN (the Institute of Physical and Chemical Research), a semi-governmental research institute.

The transfer of the Hugh collection to Japan, completed in October 1990, was very complicated as it involved the transfer of ownership and shipment of pathogenic micro-organisms across international borders and thus entailed extensive safety precautions and quarantine procedures. All of these strains are preserved and many are readily accessible to the international scientific community through JCM. In this way, a collection of biological resources at an American university was rescued thanks to a connection between experts in the relevant research field and a Japanese culture collection. However, other collections will disappear if they lack similar outside intervention. An international mechanism to perpetuate the valuable biological resources of endangered orphan collections is needed.

If, for financial reasons, BRCs are unable to perform their tasks under conditions that meet the demands of scientific research and the requirements of industry, countries will inevitably see high value-added products being transferred into a strictly commercial environment with at least two consequences:

- Blockage of access to these products or requiring payment of an exorbitant price (without taking into account the initial government research investment required to develop them).

- Definitive loss of products and elimination of technology transfer of those products for the foreseeable future.

While BRCs should be accessible to the broad scientific community, access need not be free of charge. Many collections currently charge fees to those who want to obtain biological materials and gain access to associated databases. Varying fee structures can be applied for access depending on the nature of the biological material (microbial, plant or animal resources), the status and constraints of the institution holding the resources and its relationship with the public and private sectors, national policies and relevant international frameworks. Varying fee structures and appropriate material transfer agreements can allow for the inclusion of private industrial collections of biological resources into a co-operative system of BRCs. Fee structures should take into account public investment in the development and maintenance of BRCs.

## Sources of financial support

There is no single satisfactory system of funding current culture collections that could be used as a model for global support of BRCs. A variety of funding sources that include income generation and core funding may be used to support BRCs:

- Government support.
- Private industrial support for or participation in the functioning of BRCs.
- Private industrial support for internal restricted BRCs.
- Public and private foundation support.
- Public fundraising.
- Sale of biological resources and technical materials.
- Provision of specialist services and technical consulting expertise.
- Research income (*e.g.* grants and contracts).
- Fees for repository services (*e.g.* for patent strain maintenance and safe deposits).
- Provision of technical courses.

The relative proportion of funding is likely to vary greatly. Current examples of funding range from little or no public support, the case of the American Type Culture Collection which receives only 9% of its budget from the United States government, to almost complete public subsidy, the case of Germany's DSMZ which receives about 80% of its budget from the government and only about 20% from sales of materials and services. As a result, fee structures are also likely to vary widely among BRCs, as those with little government funding will be forced to transfer the bulk of their costs to users. This can create obstacles to the exchange of cultures and harmonisation and give an advantage to users who can afford to pay for expensive strains and penalising those who cannot, particularly those in developing countries. While a uniform structure of funding is not critical, considering the different situation of public-private relations with regard to conservation and utilisation of diverse biological resources, most BRCs will require a significant government funding component, and some guarantee of continuing funding to ensure that their essential functions remain reliable for R&D and support of biotechnology.

Box 3.2. **INBio: Financing a centre for biodiversity conservation in Costa Rica through core funding and commercial contracts for bioprospecting**

Bioprospecting, the search for valuable substances for practical uses in medicine and other fields to be found from living natural resources, is one of the oldest of human activities. Costa Rica, a developing biodiversity-rich country, has recognised the opportunities offered by the link between bioprospecting and biodiversity. It has developed new ways of exploiting this linkage which have turned it into a world leader in this field. Operating on the premise that conserving natural resources into perpetuity in a tropical developing country depends in great measure upon existing knowledge of this resource, and upon society's rational use of this resource, Costa Rica launched in 1989 an innovative and pioneering project: the National Biodiversity Institute (INBio) (*Instituto Nacionál de Biodiversidad*). INBio, a non-profit organisation which seeks to maintain an *ex situ* reference collection representative of the country's biological diversity to supplement *in situ* conservation activities, receives core funding from the government and has also entered into commercial agreements to search for potentially valuable biodiversity products. INBio's strategy for commercialisation of biodiversity has focused on the development of a diversified portfolio of bioprospecting research agreements that foster innovation, learning and local capacity building. Bioprospecting agreements stipulate that 10% of research budgets for the bioprospecting activities and 50% of any future royalties be awarded to the Ministry of the Environment and Energy for reinvestment in conservation. The remaining 90% of the research budget supports national scientific and processing infrastructure and value-added activities, also oriented to conservation and the sustainable use of biodiversity. The best known achievement of INBio, which is also its most widely publicised project linking biodiversity conservation to a commercial enterprise, is a 1991 agreement signed with Merck, a pharmaceutical company, to search for naturally occurring therapeutic agents produced by plants, animals and microbes from Costa Rica's ecosystems.

The functional BRCs of the future are likely to require a mixture of core funding and varied sources of income and participation. Novel solutions may be needed, especially to keep biological resources in developing countries. (Box 3.2 discusses novel financing arrangements in Costa Rica.) Basing BRCs on commercial services alone will not suffice, because this would reduce the scope for collaboration at international level. Too much emphasis would be placed on income generation and maximisation of the local or global market share.

## Meeting the challenges

To meet the challenges of financing BRCs:

- *BRCs should be encouraged to co-ordinate their activities so as to best serve their essential functions in response to the needs of sectors that depend on their biological resources.*
- *Governments must be encouraged to provide a baseline of long-term, core funding, to centres that qualify as BRCs, to encourage high standards of quality and to promote research, development, technology transfer and commercial exploitation.*
- *Various foundations and philanthropic/charitable organisations, such as the Wellcome Trust (United Kingdom) which contributes to many biomedical and biological efforts including resource centres, the Gates Foundation (United States) and the Howard Hughes Foundation (United States), which provide support for health-related technological advances, should be asked to extend the level of support given to BRCs.*
- *Marketable products and services may be developed within BRCs, including those aimed at meeting regulatory demands and for sale to specialised customers, as long as they do not divert capacity from the core activities of BRCs.*
- *Industry should be persuaded to take a long-term view of its interests and to offer some core support for BRCs, either through funding or through direct participation in the functioning of BRCs, provided the latter maintain their independence.*
- *Efforts should be made to harmonise fee structures in situations where fees are usually charged and to see that charges are affordable for users.*

## *Chapter 4*

# ENSURING QUALITY AND EXPERTISE

BRCs need to provide greater quality assurance than is currently ensured by collections and databases. What can be done to ensure the quality of national BRCs and to establish quality assurance measures? Why is quality so important for international co-operation among BRCs? How can we deal with the shortage of personnel qualified to provide the expertise BRCs require? Transforming a collection into a national BRCs that can serve both national and international needs for materials and services requires raising the level of quality to an international standard that has yet to be defined in detail.

## Quality assurance

Users of BRCs must be guaranteed reliable, high-quality biological resources and information. They must receive the same level of service irrespective of the source of the materials or information requested. Today, however, the quality of collections of biological resources is disparate. Adequate common standards of practice which constitute "good practices" for BRCs are lacking. Although efforts to achieve internationally acceptable standards of quality are under way (Box 4.1 describes a centre that provides quality biological resources), ensuring that BRCs have the same high levels of quality remains a major task that has yet to be accomplished.

BRCs must provide access to living materials, genes and genetic elements, as well as accurate information about these biological resources. The task becomes more and more difficult as the amount and diversity of living materials to be incorporated into BRCs expands. Long-term preservation of living resources is a crucial function of BRCs. It is necessary to improve the infrastructure and to develop techniques for storing DNA samples from diverse ecosystems in which "molecular signatures" are found but the organisms themselves have yet to be cultured. Ensuring the accuracy of the genetic data associated with these living resources is a further crucial function of BRCs.

A major challenge facing BRCs is to achieve consistent naming and definitions. This is essential for communication and comparability, for assuring quality and avoiding unnecessary duplication. Consistent naming and definition are indispensable if all listings and catalogues of collections of the diversity of biological resources are to be available electronically. Guidelines, however, are lacking that would establish common platforms for communication and exchange of the data and biological materials available in BRCs. Currently, informal associations and links are provided by a number of highly specialised organisations that operate informative Web sites. The improvement of data handling and enhancement of cross-referencing will require the transformation of existing catalogues into new interconnected data structures. Maintaining the quality of data and materials and their validation will require harmonised co-ordination between BRCs and bioinformatics databases so as to provide the range of services required by the international community of life scientists and the global biotechnology industry.

Box 4.1. **The MR4: A source of quality-assured biological resources**

The Malaria Research and Reference Reagent Resource Center (MR4) was developed by the National Institute of Allergy and Infectious Diseases (NIAID) of the United States as an outgrowth of the Multilateral Initiative on Malaria, a federation of agencies involved in malaria research, control and development assistance. MR4 was implemented to meet the quality resource needs of the world scientific community engaged in R&D on malaria. The purpose of MR4 is to provide reagents to the scientific community which can be used as reference standards or to generate new renewable reagents. It provides improved access to parasite, vector and human reagents and standardisation of assays using well-characterised and renewable reagents. MR4 acquires, authenticates, preserves, produces and distributes all materials except live mosquito vectors to qualified users. These include but are not limited to parasites, antigens, antibodies, DNA constructs, RNA extracts, purified proteins and human biological materials. MR4 benefits the global community of malaria researchers by easing the burden of distribution and quality analysis of reagents and by increasing access to renewable reagents by the malaria research community worldwide. Besides reagents, MR4 provides an electronic bulletin board for users, workshops and training programmes, comprehensive online databases and printed catalogues describing the available reagents. The US government funds MR4, which is operated by the American Type Culture Collection (ATCC). There is no charge for reagents but shipping costs must be covered by the recipient. MR4 demonstrates the importance of a resource centre able to meet the quality requirements of the international scientific community.

## Expertise

The accelerating loss of the world's biological diversity through habitat destruction, pollution and ecosystem fragmentation has been accompanied by a

loss of taxonomic experts trained to discover, identify, describe and classify the world's biodiversity. Retirement of taxonomic specialists, shifts in academic recruitment and staffing and reductions in graduate training have combined to impede biodiversity research and conservation, particularly for large but poorly known groups such as bacteria and fungi. Vast numbers of species in understudied "invisible" groups constitute critical elements of food chains and ecosystems, both aquatic and terrestrial, but the high proportion of unrecognised species in these groups limits research and progress in many areas of biology and conservation.

Few experts in the fields of bioinformatics and genomics have been trained or would be available for employment by BRCs. Hence, BRCs will need to be actively involved in training and education programmes. In the 21st century, taxonomy will be strongly affected by bioinformatics and genomics, and BRCs should foster a new generation of taxonomists able to utilise informatics and molecular techniques fully. It will be very advantageous if BRCs can share expertise as well as materials and information through an integrated network (Box 4.2 describes an effort by the United Kingdom to improve co-ordination and networking at national level). Academia will also have to respond to the training needs for future staffing of modern BRCs.

Box 4.2. **The Consortium of United Kingdom National Culture Collections (UKNCC): A strategy to enhance expertise at national level**

A network of UK national collections was first established in 1947. It located collections of living organisms at centres of expertise to provide a resource for research and development. Over the years, the collections have increased their holdings to more than 70 000 microbes and cell lines and play a vital role in preserving the output of research programmes and in contributing basic materials for biotechnological development. During the late 1980s, it became clear that the conditions under which the culture collections were operating no longer fully met user demands. Among several issues of concern was the growing shortage of human resources with appropriate skills. Taxonomy and genomics, and the molecular biology relevant to both were identified as critical areas requiring development. As no single member of the network of national collections was able to address the emerging skill shortages on its own, the UK government recommended the establishment of the UKNCC as a central co-ordination mechanism for the collections in 1996. The UKNCC is co-ordinating some of the activities of the nine national collections, including collaboration among scientists working in the collections and sharing of technology and the associated human expertise. While this has met some of the initial needs, shortages of skilled manpower and expertise persist, and further efforts will be necessary to address these.

## Meeting the challenges

To achieve quality assurance, common standards of practice must be implemented that deal with the following major issues:

- *Quality management/quality assurance systems that are unified across international borders.*
- *Authenticity of biological materials, databases and bioinformatics and accuracy of labelling.*
- *Processing of cultures, cell lines, and genetic constructs, including procedures and standards for ensuring their long-term stability and quality control.*
- *Accuracy of the data collected and supplied.*
- *Expertise and training of human resources, particularly of a new generation of taxonomists able to use molecular techniques and informatics.*
- *Sharing of expertise among centres through co-ordination and networking.*
- *Use of undocumented materials and lack of citation in publications.*

## *Chapter 5*

# RESTRICTIONS AFFECTING ACCESS

To serve their intended functions, BRCs must provide appropriate access to biological resources for use in scientific R&D, the advancement of biotechnology and other uses mentioned in this report. How can legitimate access to biological resources be assured? Should everyone have access or should access be restricted? What appropriate restrictions should limit access so as to ensure safety, protect economic investments and provide ethical protection of patient rights? Which restrictions to access could and should be reduced through international harmonisation? Currently, a number of factors, including financial limitations, restrict access to the holdings of collections of biological resources. Some users are unwilling or unable to pay the fees charged by some organisations for access to biological materials and data. Other access restrictions are more fundamental, as they reflect issues of principle or are rooted in national and international laws and regulations. These restrictions concern several distinct categories:

- Protection of human, animal, plant and environmental health and safety.
- Ethical protection of the rights of individuals and patients.
- Private industry's protection of investments and industrial secrecy.
- Import/export regulations.
- Intellectual property rights (IPR) protection.
- Material transfer agreements.

All of these types of restrictions are legitimate and must be accommodated when considering access to biological resources. All reflect existing laws, regulations and practices. They all place BRCs as intermediaries between providers of biological materials and users.

Although the restrictions imposed by private industrial companies could be dealt with by internal industrial management decisions alone, restrictions that

protect intellectual property, health and safety, patient rights and confidentiality, as well as import/export regulations and material transfer agreements go well beyond the interests of BRCs and their users. They touch upon some of the most fundamental values of our society, and this will limit the ability of the interested parties alone to affect the existing regimes.

The most vexing obstacles that these restrictions will raise for the functioning of BRCs stem from the insufficient national and international harmonisation of laws, regulations, standards and practices. The exchange of biological material is subject to a variety of complex global regulatory systems (see Annex 2), including those emanating from the Convention on Biological Diversity (Box 5.1 examines some of the implications of the CBD for access to BRCs). Approximately 30 countries are currently drafting, adopting or implementing specific national legislation or provisions on access to biological resources. Achieving a single set of common rules for the utilisation and exchange of differing types of biological resources and data among BRCs will be difficult or impossible.

Legal issues concerning genetic data and bioresources are still evolving, and, for the most part, international standards have not been decided. National legislation on uses and exploitation are part of very different frameworks. Legislation relating to IPR (including information and databases), access to genetic material, exchanges (especially for plant health or other safety regulations), ethical issues (especially for human genetic material and the need for confidentiality and prior informed consent) are similarly diverse and evolving. Lack of harmonisation and consistency not only presents a challenge to BRCs and their users but can jeopardise the very goals that these laws and regulations seek to achieve. Hence, harmonisation efforts will be essential for much broader constituencies than BRCs.

BRCs can play a major role in these efforts by providing the objective data and international comparisons upon which proposals for legal and regulatory harmonisation should be based. BRCs can help users to access biological materials and data more easily by providing centralised information on differences in regulations aimed at protecting IPR and safety. A harmonised and co-ordinated international system of BRCs could provide a conduit to information on the various bodies of law that must be considered when providing access to biological resources. Specifically, BRCs should be in a position to provide accurate information on the variety of regulations for the shipment of specific biological resources and provide the guidance needed to achieve compliance with local, national and international regulations and ethical practices.

Box 5.1. **The Convention on Biological Diversity – Implications for BRCs**

The Convention on Biological Diversity (CBD) has changed the conditions governing access to biological resources. This raises the question of whether it has also changed the conditions governing access to BRCs. The CBD recognises that "the authority to determine access to genetic resources rests with the national governments and is subject to national legislation". The CBD calls upon countries to maintain their own biological resources. This may be interpreted as a requirement for *ex situ* preservation of biological resources by national BRCs to complement requirements for *in situ* conservation. A comprehensive legal analysis addressing the questions posed by the CBD for BRCs suggests that national laws and regulations will remain most important with regard to access (see Consistency with New Global Regulatory Systems in Annex 2). An international system of co-ordinated BRCs should be able to comply with the demands of the CBD as long as national laws and regulations are respected.

## Protection of human, animal, plant and environmental health and safety

Many countries have specific requirements governing the shipment, handling and possession of living resources so as to protect human, animal, plant and environmental health. Access to biological resources requires the safeguards necessary to prevent untoward consequences. This necessitates a regulatory framework that restricts access so as to ensure safety. The International Air Transport Association (IATA) regulations on the shipment and carriage of biological materials provide the overall framework governing movement of biological materials to and from BRCs. However, the myriad of non-harmonised local and national regulations presents obstacles to international exchange and the advancement of science and biotechnology and could severely handicap the role of BRCs at international level.

Particular concerns have been raised about exchanges of certain biological agents and toxins which can be misused as agents in biological warfare or bioterrorism. Some organisations have taken the precautionary step of halting exchange of biological resources that may be listed as agents for potential use in bioterrorism. The Australia Group, an informal group of 30 countries formed in 1984, develops lists of hazardous micro-organisms, toxins and equipment that could be used in biological warfare programmes, so that export controls can target specific suspect countries. Some OECD countries, such as the United States, have developed additional regulations concerning the exchange of listed agents that are considered to be dangerous pathogens and toxins that might be misused. These regulations may be affecting legitimate access by the scientific community. Ongoing negotiations in Geneva for a protocol under the Biological Weapons Convention for an international accord that may include provisions for reporting activities relative to specific agents of concern could further

restrict access to BRCs. Uncertainty about which agents are already included on restrictive lists of agents, and which may be added to or deleted from such lists, makes it difficult to ensure exchanges that will allow for continued scientific research on dangerous pathogens while maintaining national and international security. The potential for lawsuits involving alleged damage to health and safety is also causing some BRCs to restrict access to certain biological materials.

## Ethical protection of the rights of individuals and patients

The exponential growth of samples from humans for medical research and genetic testing has created new challenges for BRCs. Over the last two decades, medical research has begun to make extensive use of products of human origin in therapeutics, oncology and most recently, genetic disease. This has raised many ethical issues involving protection of confidentiality and patient rights, including issues of consent. BRCs have to be prepared for their role in transactions involving human materials and ensure appropriate expertise to guarantee protection of the rights of individuals and patients. At present, there is no agreed international system to control access to human biological resource data and biological materials of human origin and derived products that can be exchanged by BRCs and made available for wider use.

Samples and data from genetic testing challenge the technological capacities of BRCs and their ability to deal ethically with protection of the rights of individuals and patients. BRCs must be able to control access to sensitive patient data and biological samples. They must ensure that there is correct patient consent and that the identity and civil rights of donors and relatives are safeguarded. (Box 5.2 describes Iceland's pioneering efforts to combine health sector data with genealogical data and a national genetic database.) Additionally, it is essential to provide stringent quality assurance and traceability controls. Computerisation of the data must be implemented in a very strict technical and organisational environment, including cryptographic techniques.

Commercial genetic testing is offered internationally, and human samples and related data are being exchanged across national borders, particularly for research purposes, not always with the knowledge of donors. Such samples and the related genetic information can be stored in BRCs, which currently operate in the absence of clearly established international frameworks for quality assurance and the protection of security, privacy and confidentiality of such human bioresources. R&D and applied services related to genetic testing have

outpaced regulatory frameworks. International harmonisation is essential to protect patient rights and provide the necessary ethical guidelines for BRCs.

Box 5.2. **Linking Iceland's health sector to genealogical and human genomics databases**

Iceland is pioneering an effort to bridge the public and private sectors and incorporate human health data, genealogical data, genetic testing data and biological materials from patients. The effort began when the Icelandic Parliament, on 17 December 1998, approved legislation enabling the Ministry of Health and Social Security to grant a licence to create and operate an Icelandic Health Sector Database (IHD). On 22 January 2000, a licence was awarded to the Icelandic subsidiary of deCODE Genetics in Reykjavik to build and run the IHD. The IHD differs from previous projects on health or medical databases in one important respect: its nation-wide scope. This initiative has raised questions about informed consent and the ability to protect confidentiality and patient rights.

The IHD database will collect information from patient records which have undergone de-identification by coding from Iceland's national health service and store the data in a computer system for clinical and statistical analysis, with legal protection against infringement or abuse. The IHD can be linked to an existing genealogical database. The licence also permits deCODE to cross-reference IHD data with the company's genetic data, which has been obtained and analysed with the informed consent of Icelandic donors. This means the possibility of linking three databases with different forms of consent: the genealogical data base is public and requires no consent, the Health Sector Database is based on presumed consent and the genetic database requires informed consent. Ensuring privacy through encryption remains a challenge.

The linkage of genetic, health, and genealogical data will enable cutting-edge medical and genetic research, including the identification of disease genes, and the development of novel drugs and disease targets. It will enable the use of the most modern informatics technology to discover facts about health and disease through data-mining and to develop new products and services. This approach might lead to advances in the ability to analyse the interplay between genes, environment, disease, treatment and outcomes. The database should also enable Iceland's health authorities as well as industry to assess health care outcomes and the effects of existing and novel therapies and drugs. As a result, potentially useful compounds could be screened more easily, resulting in the earlier arrival of new drugs on the market.

## Private industrial investment and industrial secrecy

Many biological resources are held exclusively in industrial collections. Generally, such private industrial collections are withheld from public access to protect financial investments and industrial secrets. Private industrial biological resources typically are made accessible to the wider scientific community only when patents protect them or when they are no longer deemed to be of specific economic value. This can lead to conflict between the public and private sector

when there is a perceived need to provide access for the advancement of science and the betterment of humankind, as exemplified by the race to sequence the human genome. In that case, agreement to provide access to private and public sequence data was reached between CELERA – a private industrial company – and the human genome project sponsored by the US government only after difficult negotiations and a call for full access to the data made in 2000, by President Clinton of the United States and Prime Minister Blair of the United Kingdom. The negotiations involved in reaching the agreement to public release of the human genome sequence data highlight the challenge to be faced in trying to co-ordinate and harmonise BRCs, with the aim of providing access to biological resources in both the private and public sectors. The CELERA case points to the possibility of making some biological resources available to the public through BRCs that are not currently accessible to the wider scientific community.

### Import/export regulations

In response to economic as well as the health and safety concerns already discussed, many countries have established import and export regulations that control exchanges of specific biological materials across international borders. These regulations include requirements for licensing and quarantine that strongly affect the operations of BRCs and their ability to provide ready access to biological resources. Compliance with import/export regulations is especially complicated owing to differing national regulatory frameworks and a lack of international harmonisation. The import/export regulations can limit international exchange among BRCs and their users.

### IPR protection

Proposals to institutionalise and link BRCs internationally require close examination in terms of national and international legal requirements for ownership and protection of IPR. Any international effort to co-ordinate BRCs must recognise that intellectual property rights are primarily defined by national laws and that ownership is mainly governed by property laws. Rules and regulations governing access and exchange of biological resources are complex and depend upon the nature of the material, national legislation, the positions of countries with regard to relevant international legal agreements, such as the Budapest Treaty, and patenting and licensing policies.

The G8 Heads of State and Government at their Summit in Okinawa (July 2000), recognising IPR as a major issue for biotechnology in the post-genomics era, called for "a system of balanced and equitable intellectual property protection for gene-based inventions, based wherever possible on common practices and policies" and encouraged efforts to achieve broad harmonisation of patenting policies for biotechnological inventions.

Prior to the genomics revolution, patents and IPR protection were not a major problem for *ex situ* collections. Micro-organisms that have been patented to protect IPR are made accessible through collections under the terms of the Budapest Treaty. Without such IPR protection, both individual scientists and industry would have withheld these biological resources as "trade secrets". However, the patenting of genes and gene sequences has created an IPR-related access problem owing to uncertainties about copyright protection for databases and the implementation of stringent licensing agreements for patented genes/gene fragments.

This may greatly limit access to patented genes. Limitation of access to such biological materials and processes, which are indispensable for biomedical research, has been criticised in the United States and other countries.

## Material transfer agreements

As current national and international regimes are not sufficient to address all issues relevant to access to material, intellectual property rights and safety, institutions – including BRCs – have developed material transfer agreements (MTAs) which are legal instruments for establishing contractual relationships to define liability and to specify allowed uses of biological resources. MTAs eliminate ambiguities about the rights of use of biological materials deposited in collections. They rely on local laws to control the assignment of IPR and to specify allowable uses of biological materials and data. Because MTAs establish customised contractual relationships, they provide flexibility regarding assignment of IPR, conditions of access and permissible use. In some cases, MTAs contain provisions that would lead BRCs to restrict access.

## Meeting the challenges

To enhance access to biological resources:

- *BRCs should be accessible to all legitimate users worldwide and serve as international gateways to facilitate access to biological resources in the framework of international laws and regulations.*
- *Countries should increase their efforts to achieve greater international harmonisation of the laws, rules and practices governing access. Legal and regulatory differences among countries, particularly with regard to health and safety, use of human materials and IPR, can lead to unnecessary restriction of access to and exchange of biological materials.*
- *Private companies should be encouraged to open to the public parts of their collections that are not critical for their competitive position, either directly or through recognised BRCs.*
- *Governments must remain alert to possible negative long-term consequences of restrictive gene licensing practices on biological research and biotechnology and on the rights of BRCs to provide access to genetic biological resources, and must be prepared to address these negative consequences when they can be documented.*
- *Governments need to work towards international harmonisation of the broad variety of laws, regulations and practices aimed at protecting the health and safety of humans, animals, plants and the environment from potentially hazardous biological materials. This will discourage inappropriate uses of biological resources.*
- *Governments need to develop internationally compatible laws, standards and practices regarding human materials and data, in order to protect individual and patient rights and confidentiality, so that the ethical handling of biological materials and data from humans can be guaranteed.*

## *Chapter 6*

# TOWARDS A GLOBAL NETWORK OF BIOLOGICAL RESOURCE CENTRES

The challenges and proposals presented in the preceding chapters highlight a number of needs which governments and the scientific community will have to address at national and international level if BRCs are to fulfil their mission in the 21st century. These needs include the establishment of:

- National BRCs.
- An accreditation system based on scientifically acceptable objective international criteria.
- International linkages.
- Internationally co-ordinated and harmonised operational parameters.
- A global BRC network.

While the need for national BRCs could be satisfied at national level alone, the other needs can only be addressed at international level and call for the establishment or strengthening of international frameworks. Various international frameworks and organisations already link resource centres into networks and allow them to reach specific goals more efficiently than they could by acting alone. All these frameworks (examples of which are given in Boxes 6.2, 6.3, 6.4) are very useful and will not be weakened by moving towards a global network of BRCs.

## National BRCs

The establishment of national BRCs can help identify and address existing gaps and take advantage of opportunities not currently met by existing *ex situ* collections. They can then improve the quality of services offered and achieve efficiencies and cost savings. Achieving co-ordination between collections of bioresources through national BRCs should add value and enhance

accessibility, both nationally and internationally. National BRCs will also be needed as the nodes in the network if a global system linking BRCs is to be realised. Countries could have more than one national BRC and/or could link multiple resource centres into a national BRC (Box 6.1 presents an example of Japan's approach to establishing national BRCs). National strategies will be needed to provide adequate financial support to ensure sustainability of BRCs.

Box 6.1. **Towards the establishment of national BRCs in Japan**

Japan maintains several collections of micro-organisms and other biological resources that could become national BRCs. In addition to the existing culture collections, Japan is establishing a new national biological resource centre of industrially useful micro-organisms to meet the requirements of the life sciences and biotechnology in the 21st century.

This new centre belongs to the National Institute of Technology and Evaluation. It was created to implement a basic plan agreed by five ministries (names of ministries as of December 2000): the Ministry of International Trade and Industry, the Ministry of Agriculture, Forestry and Fisheries, the Ministry of Education, Science, Sports and Culture, the Ministry of Health and Welfare and the Science and Technology Agency. In addition, funding for the centre's infrastructure is provided by the Japan Millennium Project, which is directed by the Prime Minister. The centre will be located in Chiba Prefecture. It will be one of Japan's main national BRCs.

## An accreditation system based on international criteria

International co-operation among national BRCs requires a system for ensuring quality. This suggests the need for a system of accreditation based on international criteria with guidelines on techniques and procedures for reaching a minimum standard of quality that is transparent to the user and acceptable to the scientific community. In addition, such a system would provide emerging collections/databases a blueprint for achieving a standard that would allow them to participate in the larger network and thereby benefit a wider constituency.

It is possible to build this accreditation system on the model of existing guidelines, such as those published by the World Federation of Culture Collections (WFCC). (Box 6.2 describes the WFCC and its quality guidelines.) Although the WFCC has global reach and includes culture collections, it is not an official regulatory authority. It focuses on scientific rather than government policy issues and as such would not be the appropriate body to take this initiative forward.

Box 6.2. **The World Federation of Culture Collections (WFCC): Quality guidelines**

The World Federation of Culture Collections (WFCC), created in 1971, has more than 500 members, including culture collections in more than 60 countries. The WFCC is a member of international scientific organisations affiliated to the International Council of Scientific Unions (ICSU). It played an instrumental role in creating the regulatory framework under which the Budapest Treaty was implemented. It promotes the activities of traditional microbial culture collections by providing venues for the exchange of information about microbial collections and taxonomy. It holds plenary meetings every four years and scientific workshops and training courses once a year on average. It plays an important role in developing scientific guidelines aimed at enhancing the quality and functions of those collections and in seeking financial support for them. Quality guidelines for members of the WFCC can be found at http://wdcm.nig.ac.jp/wfcc/GuideFinal.html.

As part of its efforts to promote activities that support the interests of culture collections and their users, the WFCC pioneered the development of an international database on culture resources worldwide, the WFCC-MIRCEN World Data Centre for Microorganisms (WDCM). The WDCM provides a comprehensive directory of culture collections, databases on microbes and cell lines as well as a gateway to biodiversity, molecular biology and genome projects. The WDCM is maintained at the National Institute of Genetics (NIG) in Japan and has records of 489 culture collections in 60 countries that serve a variety of functions. The records contain data on the organisation, management, services and scientific interest of the various collections and are linked to a second record containing the list of species held.

The WDCM database forms an important information resource for microbiological activity and acts as a focus for data activities among WFCC members.

## International linkages

International linkages are essential for providing enhanced worldwide accessibility to information and biological material [Box 6.3 describes a European network linking BRCs, and Box 6.4 presents the Global Biodiversity Information Facility (GBIF), to be set up in 2001]. For networking of BRCs to be truly successful, technology for co-ordinating and combining catalogues and databases to meet the requirements of science in the post-genomics era will have to be implemented. It also will be important to co-ordinate curation, as well as development and networking of informatics tools for data analysis, comparison and visualisation. From the user's viewpoint, international linkages must meet the demand for standards of similar quality with respect to biological resources and data. Through these linkages, associated databases in various disciplines (genetics, biochemistry, etc.) could be integrated and provide rapid access to expertise. Linkage of BRCs can open up opportunities for collaborative research and technology transfer and foster education and training. Some regional networks have already been established and are moving in this

direction. CABRI, a European network of BRCs, for example, links a wide range of culture collections, databases and post-genomics BRCs. It has regulatory and policy functions that go beyond scientific exchanges but its reach is limited to EU Member States. A network with truly global linkages on the model of CABRI could eliminate the limitations on information flows and provide one-stop access to pertinent information and biomaterials for all countries.

Box 6.3. **Common Access to Biological Resources and Information (CABRI): A European network**

Common Access to Biological Resources and Information (CABRI) is a regional network linking the major European *ex situ* collections. It provides a federated database system accessible through the World Wide Web (http://www.cabri.org) and is funded in part by a grant from DGXII of the European Commission.

The project defines the tools and tests the operation of an integrated resource centre linking catalogue databases of different types of organisms, genetic materials and other "biologicals" in Europe so that, during a single search session, users worldwide can access relevant catalogues through a common gateway (and mirror sites) and request/order products. CABRI allows individual centres to maintain their own identity while sharing a single gateway for their electronic catalogues.

The centres taking part in this project currently hold 21 collections covering human and animal cells, bacteria, fungi, yeasts, plasmids, animal and plant viruses and DNA probes. Instead of having to examine a large number of databases, catalogues and other sources of information, users worldwide can check simultaneously the availability of a particular type of organism or genetic resource in many locations and order the required items once located. The quality of CABRI's service has been assessed by a technical committee and each member resource centre has contributed to defining the specifications and procedures that determine how each resource type should be handled. Entry to the network is regulated and each potential partner is evaluated against these guidelines.

The overall structure is co-ordinated by a central secretariat based in the United Kingdom.

Box 6.4. **The Global Biodiversity Information Facility (GBIF): An international network linking biodiversity databases to make them universally accessible**

The purpose of GBIF is to promote, co-ordinate, design and implement the compilation, linking, standardisation, digitisation and global dissemination of the world's biodiversity data within an appropriate framework for property rights and due attribution. Among the goals of GBIF are: *i)* developing tools and standards for accessing, linking and analysing new and existing databases, including standards and protocols for indexing, validation, documentation and quality control in multiple human languages, character sets and computer encodings; *ii)* improving the accessibility, completeness and interoperability of biodiversity databases; *iii)* developing novel user interface designs; *iv)* providing access to new and existing databases; *v)* facilitating development of an electronic catalogue of the names of known organisms.

GBIF will be established and begin operating in 2001, with approximately 20 OECD and non-OECD countries participating initially. The facility will be internationally funded and staffed by a small international secretariat. It originated in the work of the OECD Megascience Forum in 1996, but its implementation will be independent of all international organisations and it will be open to all countries. Access to GBIF data will be offered to any and all Internet users.

## Co-ordinated standards, rules and regulations taking BRCs into account.

The operational guidelines governing the essential functions of BRCs are diverse, particularly with regard to access to biological data and materials and their exchange and distribution. These rules and regulations are national or international, are issued by many different authorities, have very different degrees of enforceability and pertain to the many and varied roles of BRCs: health and safety requirements for humans, animals, plants and the environment, ethical considerations, IPR issues, import-export regulations and technical standards.

The goals of CABRI and the global BRC network are comparable; they differ mainly in their coverage and geographical reach. In contrast, the goal of GBIF – to underpin the study of biodiversity, and that of a global BRC network – to underpin the future of life sciences and biotechnology, are different. The former aims at biodiversity informatics, the second at scientific-technological progress and economic development. While these two goals are not unrelated and should not be incompatible, and while GBIF technology might become very useful for a global BRC network, neither system can replace the other. In addition to their different goals, the two systems also differ with regard to their scope, with major practical and policy implications: GBIF is limited to information flows, while the global BRC network covers not only information, but the exchange of biological materials as well.

National differences in operational parameters between BRCs significantly reduce effectiveness and increase costs. International harmonisation is therefore a priority. Given that governments are engaged in many regulatory and harmonisation efforts that may impact on BRCs it is critical that governments take into account their needs.

A global BRC network will have to be co-ordinated with existing international frameworks to establish a functional network. One is the FAO's Intergovernmental Commission on Plant Genetic Resources for Food and Agriculture. It is an example of how international organisations can help co-ordinate and harmonise the frameworks under which BRCs (in this case limited to biological resources for food and agriculture) operate. The FAO's Intergovernmental Commission links plant (and more recently also animal and micro-organism) resources across the globe to enhance the world's food security. (Box 6.5 explains this co-ordination of plant genetic resources for food and agriculture.)

Box 6.5. **International Co-ordination of Plant Genetic Resources for Food and Agriculture (PGRFA)**

International co-ordination has been achieved in PGRFA (Plant Genetic Resources for Food and Agriculture) which originated in the intrinsically "co-operative" specificity of plant breeding. The plant breeding sector has developed a tradition of conservation of interesting varieties and wild relatives of cultivated species, and of free exchange for further research and breeding of such "accessions" with common "passport data". Some networking activities – *e.g.* under the European Co-operative Programme for Crop Genetic Resources Networks (ECP/GR) – for the management of PGRFA have been established. The FAO built on this tradition, sponsoring in the 1970s the collection of PGRFA through a network of international agricultural research centres and the creation of an intergovernmental Commission on Plant Genetic Resources for Food and Agriculture (CGRFA), since widened to include animals and micro-organisms for food and agriculture, and adopting in 1983 an International Undertaking on PGRFA. In 1996 in Leipzig, the CGRFA achieved a State of the World of PGRFA and a Global Plan of Action for the conservation and sustainable utilisation of PGRFA. The International Undertaking is currently under revision to harmonise it with the Convention on Biological Diversity. Members of the CGRFA have taken this opportunity to place at the centre of the revised Undertaking a "multilateral system for facilitated access and benefit sharing", a network of *in situ* and *ex situ* PGRFA of particular importance for food security where the Parties are interdependent. It includes a global information system which identifies the PGRFA, plans and programmes for technology transfer, exchange of information, capacity building and common rules for easier access to PGRFA and allows for commercial benefit sharing. The multilateral system has gained broad support among FAO members and is intended to play a major role in the implementation of the Global Plan of Action for the management of world's plant genetic resources for food and agriculture.

The three frameworks mentioned here – CABRI, GBIF and PGRFA – are valid examples of international networks, but all are limited, each in a different way. CABRI covers all biological resources, including both material and data, but is limited to Europe. GBIF covers all types of biological information but does not cover the exchange of material. PGRFA covers both material and data worldwide, but is limited to biological resources for food and agriculture.

## A global BRC network

A global BRC network would connect national BRCs and provide the framework within which co-ordination, harmonisation and quality assurance could be provided. This would enhance the services provided to the global community by BRCs beyond what the existing international frameworks could achieve.

Specifically a global BRC network would add value by achieving the following:

- *Linkage between scientific needs and government policies.* This is why the OECD initiated this effort.
- *Provision of an international framework for regulatory initiatives.* Directly or through the appropriate national and international authorities.
- *Provision of a linking mechanism for countries lacking national BRCs.* Countries that cannot create their own BRCs would be able to link up with a global system that would help them solve at least some of their problems.
- *Enhanced efficiency.* A global BRC network would reduce redundancies and improve transparency and efficiency and thus, over time, help participants to harness resources.

## *Chapter 7*

# A CALL FOR ACTION BY OECD COUNTRIES AND BEYOND

Biological resource centres of high quality, which provide access to all legitimate users, underpin the future of the life sciences and biotechnology. To secure this essential infrastructure requires a series of actions. In most countries, the lead role will fall to national governments. Governments, however, need to act in concert with the international scientific community. Also, the private sector may play an increasing role, as its interest in BRCs is likely to grow with the global expansion of biotechnology.

Therefore, it is recommended that governments, the scientific community and the private sector work together to achieve five goals:

### 1. Establish national BRCs

Selectively seek to strengthen existing *ex situ* collections of biological data and materials and, when needed, create new collections, including in non-OECD countries, and raise those collections to the quality required for accreditation as national BRCs.

### 2. Develop an accreditation system for BRCs based on international criteria

Support the development of an accreditation system for BRCs based upon scientifically acceptable objective international criteria for quality, expertise and financial stability.

### 3. Create international linkages among BRCs

Facilitate international co-ordination among national BRCs. This should be based upon modern informatics systems that link biological data to biological materials across national BRCs and upon common technological frameworks.

### 4. Co-ordinate standards, rules and regulations taking BRCs into account

Take into account the objectives and functioning of BRCs when establishing and harmonising national or international rules and regulations. Develop policies to harmonise the operational parameters under which BRCs function, including those governing access to biological resources as well as their exchange and distribution, taking into account relevant national and international laws and agreements.

### 5. Establish a global BRC network

Support the establishment of a global BRC network that would enhance access to BRCs and foster international co-operation and economic development. A global BRC network would greatly improve the conditions under which biological materials and information are preserved and exchanged. How this challenge is met may affect the future of life sciences and biotechnology for many years to come. It is a challenge that calls for the full support of governments, the scientific community and the private sector.

*Annex 1*

## OECD WORKSHOP TOKYO '99 ON S&T INFRASTRUCTURE: SUPPORT FOR BIOLOGICAL RESOURCE CENTRES

## CONCLUSIONS AND RECOMMENDATIONS

**Tokyo, 17-18 February 1999**

### Definition of Biological Resource Centres (BRCs)

Biological Resource Centres are an essential part of the infrastructure underpinning biotechnology. They are specialised resources that acquire, validate, study and distribute collections of culturable organisms (*e.g.* microbial, plant, animal and human cells), replicable parts of these (*e.g.* genomes, plasmids, cDNA banks) and of viable but not yet culturable organisms. Most BRCs support databases that are accessible to potential users. BRCs may also provide access to data-handling tools and databases which contain molecular and physiological information relevant to their collections.

### Preamble

Biological research and development are moving forward into new areas at an unprecedented pace as we advance into the 21st century. In order to meet the current and future needs of science and technology, BRCs will be required not only to continue their current responsibilities with the best tools and infrastructure possible, but also to expand their activities to address the challenges of biology in the era of post-genomics (the applications of genomics, based on relationships between gene structure and function) and bioinformational science. Essential to the pace of change in biological science and BRCs will be the development and use of effective informatics technologies and of new technology for maintaining and storing large volumes of biomaterials. In particular, joint activities among BRCs in the areas of networking, curation, and development of informatics tools for data analysis, comparison and visualisation, would seem valuable.

To realise the benefits of BRCs, each Member country should consider developing a policy for BRCs that recognises their value. This policy may be co-ordinated across ministerial departments and other funding bodies, and should take into consideration collaboration and financial support for national, regional and international facilities. This policy should encompass service centres, generalised as well as specialised collections, associated data sets, bioinformatics systems, as well as the acquisition,

evaluation and dissemination of information and materials, all of which are important aspects of BRCs.

**Points of principle for action by Member countries**

The OECD should encourage Member countries to:

- Recognise the traditional and continuing important role of, and need for, BRCs in science and technology:
    - By developing and implementing co-ordinated government policies and programmes to support BRCs in their own countries and/or regions according to need.
    - By providing sustainable funding and support to allow BRCs to function according to international best practices as evaluated by the scientific community.
    - By fostering co-operation and collaboration among BRCs for the development of an integrated global resource.
    - By maximising the benefits to be derived from BRCs, facilitating their integration into networks at national, regional and international levels.
    - By developing mechanisms for the preservation of large numbers of diverse biomaterials.
- Recognise the opportunities and challenges facing BRCs in the 21st century:
    - By developing mechanisms for the effective utilisation of information technology in order to process the data being accumulated at an unprecedented pace in biological sciences.
    - By fostering joint activities among BRCs in the areas of networking, curation, development of informatics tools for data analysis, comparison and visualisation.
    - By integrating relevant information from biological science research and genomics into a comprehensive information system for BRCs.
    - By ensuring co-ordination and complementarity to ongoing international efforts including the Global Biodiversity Information Facility (GBIF) proposed by the OECD Megascience Forum.

The Delegates attending the OECD Workshop Tokyo '99 on Scientific and Technological Infrastructure (Support for Biological Resource Centres) recommend that the Working Party on Biotechnology (WPB) establish a Task Force on Biological Resource Centres whose mission is to drive forward the recommendations listed below. The Task Force should report to the WPB by the end of the year 2000.

### 1. Sustainability – ensuring the long-term survival of BRCs

- Consider funding strategies that can be used in support of BRCs.
- Consider review processes for assessing the value of functions performed by BRCs.

### 2. Acquisition and distribution – ensuring scientific progress through access to contents of BRCs

- Consider the appropriate contents of BRCs and criteria to encourage the timely deposition of key biological materials and data so as to realise the benefits of mutual research investment.
- Consider harmonised criteria for the safe and scientifically based national, regional, and international distribution of biological materials and associated data, based on a rational assessment of risks. These would include appropriate import, export, and shipping policies for the distribution of dangerous pathogens, and should also ensure that these do not fall into the hands of non-legitimate users.

### 3. International linkage – ensuring co-ordination and complementarity of BRCs

- Consider the value to the scientific community of a tiered networking structure to facilitate the co-ordination of BRCs at national, regional and international levels.
- Consider policies that would:
  - Facilitate the construction of an "international BRC" with electronic ("virtual") linkages among BRCs.
  - Create a distributed system that would be sufficiently flexible to enhance the diverse strengths and utility of each contributing BRC.
  - Integrate relevant information from biology research and genomics into a more comprehensive and useful information system for BRCs.

### 4. Quality and efficiency – ensuring enhanced effectiveness of BRCs

- Consider the scientific and technological tools and management systems necessary to meet the future needs of BRCs including the required minimum level of infrastructure that would ensure the highest quality of BRCs with respect to services, information, and materials.
- Consider guidance to reduce unnecessary duplication in holdings and services that facilitates appropriate specialisation and support of scientific R&D.

### 5. Research and expertise – ensuring education, training and research within BRCs

- Consider policies that foster and enhance the performance of research in BRCs including collaborative relationships.
- Consider policies to support training and education to maintain and extend the necessary expertise, including systematics, curation, research and bioinformatics.

*Annex 2*

## CONSISTENCY WITH NEW GLOBAL REGULATORY SYSTEMS

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Several global regulatory systems may impact on the BRC initiative, especially with regard to its international networking part. Consistency needs to be analysed on the basis of three main points.

### The legal status of biological resources

The legal global framework for biological resources is given by the Convention on Biological Diversity which provides, under Article 2, the definitions of biological resources ("includes genetic resources, organisms or parts thereof, populations, or any other biotic component of ecosystems with actual or potential value for humanity"), genetic resources ("means genetic material – meaning any material of plant, animal, microbial or other origin containing functional units of heredity – of actual or potential value"), and, according to Article 3, puts their exploitation under national sovereignty. As a consequence of this principle of national sovereignty, the legal status of biological resources (national heritage, subject to private property, public domain, etc.) results from national law.

### The legal status of collections of biological resources

Few collections of biological resources are defined internationally: this situation appears only for deposit or reference collections in the context of intellectual property rights, according to the Budapest Treaty on the international recognition of micro-organisms deposit (defined by Articles 6 and 7) or to the UPOV Treaty on plant variety protection which provides for a "service" under Article 30.1 (without stating precisely its status and detailed obligations).

### Activities undertaken on biological resources

BRCs are mainly concerned by international regulations on conservation, utilisation and exchange of biological resources.

On conservation, the most relevant provision for BRCs is given by Article 9 of the Convention on Biological Diversity on *ex situ* conservation: "Each Contracting Party

shall, as far as possible and as appropriate, and predominantly for the purpose of complementing *in situ* measures:

a. Adopt measures for the *ex situ* conservation of components of biological diversity, preferably in the country of origin of such components.

b. Establish and maintain facilities for *ex situ* conservation of and research on plants, animals and micro-organisms, preferably in the country of origin of genetic resources.

c. Adopt measures for the recovery and rehabilitation of threatened species and for their reintroduction into their natural habitats under appropriate conditions.

d. Regulate and manage collection of biological resources from natural habitats for *ex situ* conservation purposes so as not to threaten ecosystems and *in situ* populations of species, except where temporary *ex situ* measures are required under subparagraph (c) above.

e. Co-operate in providing financial and other support for *ex situ* conservation outlined in subparagraphs (a) to (d) above and in the establishment and maintenance of *ex situ* conservation facilities in developing countries."

These provisions are consistent overall with the OECD initiative on BRCs: they do not include specific obligations on the modalities of conservation, except for a focus on the country of origin of genetic resources. If the global BRC network relies on national BRCs maintaining genetic resources that are under national sovereignty and responsibility, there will be no inconsistency on this point with the CBD. It should be noted that these provisions do not apply to biological resources from human origin, giving BRCs more freedom on their conservation.

On utilisation, the CBD provides only general provisions on the sustainable utilisation of components of biological diversity (Article 10), focused mainly on *in situ* biological diversity. The global regulatory framework on intellectual property rights (IPR) will certainly have a larger impact on the design and functioning of BRCs. The patentability of biological material is addressed, explicitly for plant, animal and microbial domains, implicitly for the human domain, by Article 27 of TRIPs (Trade Related Intellectual Property Rights Treaty, Marrakech, 15 December 1993). The rights granted to the holders of such property rights are defined under Article 28.1, including the right to prohibit others to manufacture, use, propose to sell, sell or import for these purposes the product protected. If BRCs include such protected biological material, this provision will apply. It should be recalled that intellectual property rights are implemented through national laws, which may differ from one country to another in terms of the detailed provisions, especially on the protection of data and databases, on the "research exemption" which is of particular importance for BRCs. In addition to IPRs, some national or regional regulatory systems may apply, especially in the human

domain, with regard to ethics in research and commercial utilisation of parts or components of the human body. Then, for utilisation, the CBD provides a general obligation (Articles 3 and 15) for sharing "the results of research and development and benefits arising from the commercial and other utilisation of genetic resources with the Contracting Party providing such resources". The practical implementation of this provision is mainly considered when addressing the exchange of biological material.

The exchange of biological material is subject to a large number of global regulatory systems. Article 15 of the CBD recognises that "the authority to determine access to genetic resources rests with national governments and is subject to national legislation". About 30 countries are currently drafting, adopting or implementing specific national legislation on access or provisions on access under biodiversity national legislation. They usually explicitly cover plant, animal and microbial genetic resources and provide for procedures and modalities of "prior informed consent" for acquiring biological material and of benefit sharing. The Conference of the Parties to the CBD of May 2000, in Nairobi, decided to initiate in October 2001 an open-ended working group on access and benefit-sharing, "with the mandate to develop guidelines and other approaches for submission to the Conference of the Parties and to assist Parties and stakeholders in addressing" elements relevant to access and benefit sharing (Decision V/26).

A specific global regulatory system is currently being developed under the auspices of the FAO for plant genetic resources for food and agriculture. The prompt adoption of the International Undertaking is planned for the future and will provide for genetic resources relating to a list of plant genera/species or crops considered as important for food and agriculture, a regime of facilitated access (Article 13) and benefit sharing (Article 14) that would apply to all parties to the International Undertaking.

- The CBD Cartagena Biosafety Protocol adopted in January 2000 in Montreal (not yet entered into force as at February 2001) provides a specific procedure (Articles 7-10, and 12) for the "advanced informed agreement" for international exchange of living modified organisms for intentional introduction into the environment, that should not apply (Article 6) to the "transboundary movement of living modified organisms destined for contained use" (mainly for research purposes), as long, however, as this movement is in accordance "with the standards of the Party of import".
- On micro-organisms, different rules for the exchange of biological materials, according to the degree of pathogenicity of micro-organisms, are already implemented routinely by holders of collections and will not raise problems for exchange of biological material between BRCs.
- Few international regulations would apply to the exchange of information between BRCs (Article 39 of TRIPs relating to non-divulged information). They will mainly have to deal with national legislation on the protection of human being and personal privacy, including on nominative data.

Generally speaking, BRCs will have broad leeway to organise the conservation of biological resources. For the utilisation of the biological materials and information they manage, national BRCs will have to check the consistency of the modalities of planned activities in the global BRC network with relevant national legislation. For the exchange of material and information, global regulatory systems relating to different categories of biological resources are already in force (micro-organisms), under construction (International Undertaking on Plant Genetic Resources for Food and Agriculture, guidelines to implement the general provisions of the CBD) or waiting for entry into force as at February 2001 (CBD Biosafety Protocol). It seems difficult to consider single common rules for the utilisation and exchange of biological resources and data between BRCs. Such rules will ultimately depend on the nature of the material concerned, on the legal situation of countries involved with regard to these international agreements, in some cases on the intended use of the biological material, and to a large extent, on national legislation or standards.

*Annex 3a*

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*Annex 3b*

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# Biological Resource Centres

## UNDERPINNING THE FUTURE OF LIFE SCIENCES AND BIOTECHNOLOGY

Biotechnology and the genomics revolution are changing our world's scientific-technological and socio-economic framework. A new type of raw material – one invisible to the naked eye – will become the essential ingredient of the life sciences and biotechnology and of our future: it is the living cell – human, animal, plant or microbial – and the genes it contains. Who keeps, owns, distributes and sells this raw material? Who has access to it? What are the ethical implications of dealing with human cells and DNA?

This book sheds light on many of these questions. It identifies the main challenges and how they can be met.



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