OECD BEST PRACTICE GUIDELINES FOR BIOLOGICAL RESOURCE CENTRES



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FOREWORD

In order to meet modern demands for the further advancement of biotechnology and life sciences, the OECD in 2001 introduced a new concept of repositories and providers of high quality biological materials and information: Biological Resource Centres (BRCs). BRCs are considered to be one of the key elements for sustainable international scientific infrastructure, which is necessary to underpin successful delivery of the benefits of biotechnology, whether within the health sector, the industrial sector or other sectors, and in turn ensure that these advances help drive growth.

As a step forward, in 2001 experts from OECD countries came together and agreed a consensus report that called upon national governments to undertake a number of actions to bring the BRC concept into being in concert with the international scientific community.

This report presents the outcome of discussions held by the OECD member countries, together with a number of key partner countries, under the auspices of an expert Task Force established by the OECD Working Party on Biotechnology, following recommendations made in the 2001 report. Specifically, a series of best practices for BRCs were developed in extensive consultation with the scientific community.

These best practices are intended to serve as a target for the quality management of collections. Achieving the levels of quality associated with full compliance with these best practices should be regarded as the pinnacle of success. But few BRCs will reach these levels of quality, even today, some six years after publication of the original OECD call for action. Rather, the best practices set out in this report are meant to provide guidance for those that seek to improve the quality of BRCs, but in many cases this will remain – at least to some extent – aspirational.

The OECD Working Party on Biotechnology agreed the best practices set out in this document at its 21st Session on 19-21 February 2007 and they were subsequently endorsed by the OECD's Committee on Scientific and Technological Policy (CSTP) at its 89th CSTP meeting in March 2007.

We are grateful to all participants in the Task Force on Biological Resource Centres (see Annex I) for their considerable efforts in developing these best practices and, in particular, to Japan, France and the United Kingdom for financial and/or logistical support.

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PREFACE

This document comprises the report of the Task Force on Biological Resource Centres (TFBRC) on best practice guidelines for BRCs. The report comprises two main parts. Part I sets out the background and rationale to the project as well as describing the methodology used for the articulation of best practice guidelines. A number of general recommendations (principally related to the implementation and review of the best practice guidelines) are set out in Chapter IV. Part II of the report comprises the best practice guidelines themselves. Four sets of best practice guidelines are included dealing with *(i)* general quality aspects, *(ii)* biosecurity-related issues, *(iii)* specific guidelines for BRCs holding and supplying micro-organisms, and; *(iv)* specific guidelines for BRCs holding and supplying human-derived materials. A fifth section in Part II provides optional best practice guidelines on the establishment of national certification systems related to the best practices.

Part I

RATIONALE AND DEVELOPMENT OF THE PROJECT

CHAPTER I – INTRODUCTION

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.

Such biological resources are the source materials for scientific investigation and R&D that lead to discoveries that will support the progress of biotechnology and the bio-industries. Ensuring the proper maintenance and supply of biological resources is thus essential for the future advancement of biotechnology and its contribution to the growth of the bioeconomy.

In order to meet modern demands for advancements of biotechnology and life sciences, the OECD in 2001 introduced[1] a new concept of repositories and providers of high quality biological materials and information: the Biological Resource Centre.

Biological resource centres are:

> *"an essential part of the infrastructure underpinning biotechnology. They consist of service providers and repositories of the living cells, genomes of organisms, 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 data bases containing molecular, physiological and structural information relevant to these collections and related bioinformatics. BRC 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".*

Thus BRCs are fundamental to harnessing and preserving the world's biodiversity and genetic resources and serve as an essential element of the infrastructure for scientific investigation and R&D. BRCs serve a multitude of functions and take on a range of shapes and forms. Some are large national centres performing a comprehensive role providing access to diverse organisms. Other centres play much narrower, yet important, roles, supplying limited but crucial specialised resources.

The development, expansion and survival of these BRCs continue to face many challenges. These include those posed by the molecular revolution (genomics and the information revealed by DNA

1. "Biological Resource Centres: Underpinning the Future of Life Sciences and Biotechnology", ISBN 92-64-18690-5, 2001, OECD, Paris.

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.

We now see 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 21st century is already seeing an explosion in the availability of heterogeneous biological materials as well as mostly increased amounts 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.

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.

The Experts from the OECD countries therefore came together in an initiative designed to secure this essential infrastructure. They agreed a consensus report in 2001 that called upon national governments to undertake a number of actions in concert with the international scientific community, including[2]:

i) Selectively seek to strengthen existing *ex situ* collections of biological data and materials and create collections of new resources, including in non-OECD countries.

ii) Facilitate international co-ordination among BRCs by creating an agreed system of linkage. This should be based upon modern informatics systems that link biological data to biological materials across BRCs and upon common technological frameworks.

iii) Take into account the objectives and functioning of BRCs when establishing and harmonising national or international rules and regulations.

iv) 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.

v) Support the establishment of a global BRC network that would enhance access to BRCs and foster international co-operation and economic development.

2. The experts also envisaged that a global BRC network should be based on a system of accreditation for BRCs.

These recommendations were subsequently echoed by the meeting at Ministerial level of the OECD Committee for Scientific and Technological Policy (CSTP) in January 2004.[3]

This report presents the outcomes of considerations by the OECD member countries, together with a number of key partner non OECD countries[4], under the auspices of a specialist Task Force established by the OECD's Working Party on Biotechnology, related to a number of these recommendations in the 2001 report. Specifically, a series of best practices for BRCs were developed in extensive consultation with the scientific community. The best practices are intended to serve as a target for the quality management of collections. Achieving the levels of quality associated with full compliance with these best practices should be regarded as the pinnacle of success. But few BRCs will reach these levels of quality, even today, some six years after publication of the original OECD call for action. Rather, the best practices set out in this report should be conceived of as guidance for those that seek to improve quality of BRCs, but in many cases these will remain – at least to some extent – aspirational.

This report does not, however, address the facilitation of international co-ordination among BRCs by creating an agreed system of linkage, nor the establishment of a global BRC network. It is expected that these issues, together with a preliminary assessment of the impact of OECD work in this area, will be the subject of a third and final OECD report on BRCs, likely to be published in 2008.

This report consists of two parts: Part I provides background to the project and the rationale for the approach taken as well as a summary of the methodology used. Part II consists of negotiated and agreed best practices for BRCs.

3. OECD (2004) « Biotechnology for Sustainable Growth and Development »; communiqué of meeting of CSTP at Ministerial level 29-30 January 2004.

4. See Annex I.

CHAPTER II – THE FUNCTIONS OF BIOLOGICAL RESOURCE CENTRES (BRCs) AND THE QUEST FOR QUALITY AND SUSTAINABILITY

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 Reference Material.
- 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 reference material

An increasing number of test methods rely on the use of certified, stable and validated biological materials. A small but rising number of BRCs are seeking and achieving certification for the supply of such biological reference material.

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 repositories of biological resources for the purpose of both implementing IPRs, and in some cases, supporting the enablement (*e.g*. the United States) or description (*e.g*. European Union/Japan) for patentability. 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 referenced in the EU Directive on the Legal Protection of Biotechnological Inventions. IDAs, as defined in the Budapest Treaty, sometimes maintain secrecy about the deposited resources. However, when a deposit of biological material is required by a patent office in order for an invention to be considered patentable, the depositor must remove any confidentiality requirements and must agree that the IDA may furnish samples of deposited materials to third parties.

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 best practice 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.

Not all BRCs fulfil all of these functions, although some do. BRCs are heterogeneous by nature, and that heterogeneity should be recognised and respected. Even the most modest specialist collection may play an essential role in the developing bioeconomy.

1. Quality of biological resources

1.1. Need for high quality biological materials

The 2001 report concluded that there is a need for BRCs to provide greater quality assurance than is currently exercised by culture collections and databases. It asked; what can be done to ensure the quality of national BRCs and to establish quality assurance measures; why is quality so important an underpinning for international co-operation among BRCs; how can we deal with the shortage of qualified personnel needed to provide the expertise required by BRCs? It concluded that transforming a culture collection into a BRC that can serve both national and international needs for materials and services requires elevating the level of quality to an international standard that had yet to be defined in detail.

The 2001 report made clear that, users of BRCs must be guaranteed reliable, high-quality biological resources and information. The ultimate goal should be that they receive the same level of service irrespective of the source of the materials or information requested. In 2001, however, as is the case today, the quality of collections of biological resources was disparate. Adequate common standards of practice which constitute "good practices" for BRCs were and are lacking.

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. Best practice 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.

There is an ever-increasing demand for biological materials of quality. This may be a key driving force for the business elements of a collection's strategy for long-term sustainability, and is also an increasing requirement to attract funds for high quality scientific research.

1.2. Quality management

In order to consistently provide biological materials of quality, BRCs need to improve their management systems to control the quality of biological materials and related data that meet specific criteria and applicable regulatory requirements.

Used correctly, improved quality management will provide a better product that can be used to attract investment in the development of culture collections, and the outcome will be beneficial to all stakeholders.

2. Financial sustainability

The long-term stability of BRCs requires adequate and reliable sources of funding. But 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. The promise of biotechnology is inextricably linked to appropriate support of BRCs.

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 a high price (which may not take account of the initial public 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.

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. 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.

Thus the implementation of quality assurance and quality management of BRCs as well their long-term sustainability require adequate and reliable sources of funding. Funding issues form the main barrier impeding culture collections to fully contribute to the economy.

However, the diversification of activities in moving from the "Culture Collection" model to a BRC holds out the expectation of additional sources of revenue, both from existing activities and projects related to new technology based partnerships. BRCs include a variety of activities directly related to quality control, collection development and operation that may include opportunities for some additional cost recovery activities. Among several potential new sources of revenue is the generation of genomics and proteomics data that complement and add value to biological materials themselves. However, the degree to which such activities may actually provide support sufficient to ensure financial sustainability of a BRC is unproven.

Nevertheless, 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. Having said this, it is to be expected that most BRCs, whether single large national centres or smaller distributed or specialized centres, will require some degree of commitment to core funding which could include their respective national governments. Other kinds of funding sources include support from industry, grants from agencies that support research, cost-recovery through fees-for-service, development of databases and other tools that complement the core role of BRCs, and even funding from charitable sources, especially those associated with public health or sustainable development.

Current examples of funding range from little or no public support to complete public subsidy. 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 (see Table 1).

Governments will wish to consider the extent to which funding can be used as an instrument to encourage collections to strive to meet BRC best practices. This would encourage high standards of quality and promote research, development, new technology and commercial exploitation.

Various foundations, including public fundraising and public and private foundation support (for example), as well as philanthropic or charitable organizations might review whether then can extend the level of support given to BRCs.

Industry needs to take a long-term view of its interests and to offer core support for BRCs, either through funding or through direct participation in the functioning of BRCs.

Marketable products and services may be developed within BRCs, including those aimed at meeting regulatory demands and for sale to specialised customers.

The needs and capacities of individual countries vary, and the needs of developing countries must be understood and accommodated. The strategy should be to identify collections and centres already capable of improving quality as envisaged in BRC best practices or forming a network, and build upon and improve these rather than starting up new BRCs, especially in developing countries where resources are limited.

Table 1. Existing and Potential Income Streams for BRCs

Existing	Potential
Government support	cDNA libraries, genomic libraries, filter sets, clones, plates, PCR products
Private industrial support for participation in the functioning of BRCs	Microarrays and reagents
Private industrial support for internal restricted BRC activities	RNAi resources
Public and private foundation support	Accreditation/standardization-added value products and services
Public fundraising	Data storage and retrieval
Sale of biological resources and technical materials	Software development/collaborations - data mining tools
Provision of specialist services and technical consulting expertise	Technology development/collaborations-LIMS/robotics
Research income (grants and contracts)	Sequence database annotation/phenotypic analysis
Fees for repository service (safe deposits and patent strain maintenance)	Linking genomics databases to proteomics
Provision of technical courses	MLST (multilocus sequence typing) - population studies
Exploitation of and adding value to genetic resources	

The development of a global BRC network would be an important and useful step in ensuring cooperation, review and implementation of best practices and development of additional funding mechanisms.

3. Training

The 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.

BRCs will thus face challenges linked to their daily operations. For example, BRCs deal with state-of-the art methodologies for preservation, replication and quality control of biological material and the competent use of such methodologies needs to become a part of the professional culture of BRCs. Similarly, BRCs face challenges in the consistent use of naming and definitions. This is essential for communication and comparability, for assuring quality and avoiding unnecessary duplication. Moreover, staff of BRCs should aim to become familiar with documented protocols and comply with the policies and procedures laid down in the BRC best practices for quality management.

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. Academia will also have to respond to the training needs for future staffing of modern BRCs.

4. Towards best practices

To achieve quality assurance in BRCs, best practices for quality are clearly needed. To achieve the highest levels of quality, such best practices need to be fully implemented and monitored, but even partial implementation should bring with it quality improvements. Such an approach will lead to achievement of the following objectives:

- International unified quality management/quality assurance.
- Authenticity of biological materials, databases and bioinformatics and accuracy of labelling.
- Assurance of long-term stability and quality control of cell cultures, cell lines, and genetic constructs, including procedures and standards.
- Accuracy of the data collected and supplied.
- Raising of expertise of human resources, particularly of a new generation of taxonomists able to use molecular techniques and informatics.
- Potential for sharing of expertise among centres through co-ordination and networking.

OECD best practices for BRCs have been developed by an expert Task Force under the Working Party on Biotechnology.

CHAPTER III – DEVELOPMENT AND IMPLEMENTATION OF BEST PRACTICES FOR BIOLOGICAL RESOURCE CENTRES (BRCS)

1. Introduction

OECD countries agreed in 2001 that BRCs need to provide greater quality assurance than was then ensured by collections and databases. At the time, they posed a fundamental question – what can be done to improve the quality of BRCs.

This chapter of the second OECD Report on BRCs addresses this specific issue; by what means can quality be raised so that there is a shared international set of goals for maintenance and supply of biological materials?

The approach taken by the OECD countries, plus their partners[5] was to develop a series of best practices articulated as quality guidelines. This chapter describes the general approach to best practice taken by the participating countries, summaries the key elements of each of the individual guidelines on best practices agreed, considers some options for implementation of such best practice and provides a degree of insight into the likely costs of compliance.

The Best Practices themselves, which have been agreed by all 30 OECD member countries, plus a number of important partner countries, are set out in Part II of this report.

2. Building consensus on best practice guidelines

The Best Practices set out in Part II of this report were developed by a group of national experts brought together as a Task Force on Biological Resource Centres, under the auspices of the OECD's Working Party on Biotechnology. The Task Force was chaired by Mr. Louis Rechaussat (France). Besides the OECD countries, a number of non-member observer countries (China, Russian Federation, South Africa) participated in the Task Force, as did invited experts from a range of other countries that the Task Force considered could lend particular expertise. The full range of participants is set out in Annex I.

The Task Force was clear from the outset that the potential user community should be as involved as possible in identifying and formulating best practice. The Task Force therefore made considerable effort to reach out to the various communities as their thinking progressed. They did this principally in three ways:

Face-to-face engagement: Where Task Force experts ran a number of open meetings in the margins of major international conventions of those involved in collection management that sought to encourage broad awareness of the OECD work on BRCs as well as specific input on the detail of best practices.

Broad, written consultation: Consultation sought comments from a broad range of stakeholders on practicality, implementation and technical accuracy of BRCs quality guidance. Around 500 stakeholders were consulted.

5 . See Annex 1.

A pilot study on the best practice guidelines: A pilot study was run to test out the validity and operability of the draft best practice guidelines (which were refined in light of this). More details are provided in the next section.

3. Pilot study on best practice guidelines

The goal of the pilot study was to test the validity and practicality of the OECD general and domain specific best practice guidelines.[6] The study achieved the following main objectives:

- To ensure broad consultation on best practice guidelines with relevant stakeholders as well as national and international bodies.
- To test the validity of the best practice guidelines and their applicability to existing culture collections.
- To assess the impact of best practice guidelines on the functioning of culture collections.
- To identify a range of available options for those entities that wish to implement the best practice guidelines in full.
- To perform a preliminary cost benefit analysis for collections applying the best practice guidelines.

The pilot study was performed by a group of stakeholders including culture collections, research institutes, certification/accreditation agencies and international organisations. All comments and outputs from the pilot study assessment were taken into account in the best practice guidelines set out in Part II.

More details of the methodology used for public consultation and the pilot study are provided in Annex II.

4. General structure of the best practice guidelines for the operation of BRCs

The guidelines for the operation of Biological Resource Centres (BRCs) which are set out in Part II of the report together provide the basis for best practices in the management of BRCs.

Two sets of general guidelines address all Biological Resource Centres, no matter what type of biological material they hold and supply. These are: *General Best Practice Guidelines for all BRCs* and *Best Practice Guidelines on Biosecurity for BRCs*. Further guidelines provide additional best practices for those BRCs that hold and supply biological material within specific domains. Best practice is achieved when BRCs comply with all sets of general guidelines applicable to the specific domain that the biological materials they hold and supply belong to. Currently two sets of such OECD Best practice guidelines exist: *Best Practice Guidelines for the Micro-Organism Domain*, and *Best Practice Guidelines for Human-Derived Material*. Further domain-specific best practice guidelines for animal and for plant material are regarded as necessary, and might be developed under the auspices of a future global BRC network.

Where elements addressed in best practices are covered by existing national and/or local laws and regulations, such laws and regulation must take precedence.

6. See “General Structure”.

4.1. General Best Practice Guidelines for all BRCs

The *General Best Practice Guidelines for all BRCs* give general best practice for the acquisition, maintenance and provision of biological materials and on the management of Biological Resource Centres as defined by the OECD. The initial input was provided from the Common Access to Biological Resources and Information (CABRI) Guidelines and the UK National Culture Collection (UKNCC) Quality Management System. It has been adapted to meet the needs of the user community.

The general best practice guidelines cover all areas of best practice addressed by the more specific stand-alone best practice documents, albeit at a more general level. Included within the scope of best practices are: definitions (all of which apply to subsequent more specific best practice documents); organisational requirements (sustainability, management, training); premises (including maintenance and access); equipment; document management; data and informatics; media and reagent preparation; accession, preservation, maintenance and supply of deposits and; quality audit and review.

4.2. Best Practice Guidelines on Biosecurity for BRCs

Many BRCs are entrusted with the maintenance and exchange of hazardous biological resources. Society confers trust in BRCs as custodians of such materials, demanding the responsibility is taken for their safe use. In this context, culture collections have long recognised the duties of implementing proper containment procedures for hazardous biological material to safeguard workers against accidental exposure and acting in accordance with legislation on export controls and transport safety measures. More recently, the menace of bio-terrorism has changed the geo-political landscape, and consequently facilities that handle materials and information that could potentially be of "dual-use" have the added responsibility to make special efforts to secure against loss or theft.

The prospect of bioterrorism gives rise to the need to protect facilities that work with, store or transfer dangerous biological material from being intentionally misused for malevolent ends. Thus, to contribute most effectively to scientific and economic development, BRCs should not only promote scientific openness but also a sense of security.

To deliver such a balanced and mutually reinforcing effect the aim of *Best Practice Guidelines on Biosecurity for BRCs* is to reduce the probability that dangerous biological material could be obtained by unauthorised persons and deployed to cause harm, without unduly hindering research or being financially burdensome. Such principles should be clearly articulated and grounded in an understanding of the biological material and the operations of BRCs.

The *Best Practice Guidelines on Biosecurity for BRCs* are provided to support governments in the recognition of BRCs, and describe the methods and protocols for secure maintenance and provision of biological materials. They should be implemented in conjunction with the *General Best Practice Guidelines for all BRCs* and the applicable specific domain guidelines for BRCs.

The *Best Practice Guidelines on Biosecurity for BRCs* are designed to secure all types of biological materials (*e.g.* plant-, animal-, micro-organism- and human-derived) in proportion to the risk they present, and thereby marginalise any obstacles that BRCs might face in carrying out their function to provide quality assurance and rapid supply of biological materials for research, public health and economic development. Tailoring the level of security measures to the actual needs of diverse BRCs implies the utilisation of a mechanism capable of identifying which biological materials need to be secured. To address this fundamental point, some countries have

adopted a list-based approach to biosecurity, whereby a list is established of biological materials that are deemed in need of special security measures and there is a clear and absolute distinction between those organisms that are on the list – and require specified additional security measures – and those that are not, and hence require no additional security above and beyond what is normally in place at facilities.

Given the risk of mistakenly excluding a hazardous biological material from such a list, the *Best Practice Guidelines on Biosecurity for BRCs* adopt an approach consisting of two key components: performing a risk assessment of the various biological materials held in collections and recommended risk management practices to reduce the risk of their loss or theft. The first key component assigns materials to one of four biosecurity risk levels: high, moderate, low or negligible, according to the degree of risk the biological material presents. The second key component contains measures tailored to the level of biosecurity risk that a biological material presents. Applying a graded approach is intended to better target the resources allocated to security by BRCs and to avoid establishing excessive security measures.

These best practice guidelines are intended to apply to all BRCs, irrespective of the type of material they hold and supply. However, given that the principal target is the biosecurity of pathogens, the best practice guidelines will in particular apply to micro-organism domain BRCs.

4.3. Best Practice Guidelines for the Micro-Organism Domain

Microbial biological resources have been increasingly recognised for their fundamental role in underpinning research and analysis in many scientific disciplines, as well as applications in biotechnology and industry. Many countries have developed national microbial collections to meet their scientific and industrial needs.

Given the increasing amount of new microbial resources used for the scientific and industrial purposes and internationalisation of science and research, there is an increasing demand of creation of internationally agreed best practices to leverage quality assurance of micro-organisms. Such best practices should help ensure quality management, quality control, secure exchange of micro-organism and derived materials and related information and data, staff training, protection of Intellectual Property Rights (IPRs) and sustainability of culture collections.

To address the above items, the OECD developed *Best Practice Guidelines for the Micro-Organism Domain*. The purpose of this document is to help ensure that micro-organisms held and supplied by BRCs are of the highest standard and authentic. The methods used should be such that the key features of micro-organisms maintained are retained and should ensure their consistency amongst BRCs supplying them. This will help to provide a reliable basis for research and development in different laboratories and will contribute towards protection of the health of laboratory personnel, the public and the environment. The best practice guidelines largely follow the scope and format of the *General Best Practice for all BRCs*.

4.4. Best Practice Guidelines for Human-Derived Material

In the post-genomics era, human-derived biological resources for basic research use in general and applied science constitute a vital tool for clinical, health-related biotechnologies and the development of new pharmaceuticals, medical devices, diagnostics and therapies.

Human-derived biological materials thus represent an important basis for the advancement of biomedical and pharmaceutical sciences.

The OECD countries are united in their ambition to improve the efficiency and effectiveness of health-related innovation in biotechnology and to provide a predictable policy environment for the use and exploitation of human genetic information. These goals were endorsed both by the science and technology, as well as the health ministers, of the OECD member countries during two separate ministerial meetings in 2004.

The OECD, through its Working Party on Biotechnology, has a significant programme of work addressing these issues, and the OECD's Governing Body – the OECD Council – has recently adopted two international legal instruments related to the exploitation of human genetic inventions and the quality assurance of the generation and exchange of human genetic information through genetic tests.

The OECD report on BRCs noted that:

> *"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. 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".*

Since then, the OECD has adopted Council Guidelines on Licensing of Genetic Inventions (thus dealing with the IPR-related issues referred to above) as well as Council guidelines on Quality Assurance in Genetic Testing (thus dealing with issues related to generation and exchange of genetic information). Further Guidelines on Maintenance and Governance of Human Genetic Research Databases are forthcoming.

The BRC Task Force therefore sought to address the last of the issues addressed above, namely the maintenance and exchange of living human-derived materials.

The OECD thus developed best practice guidelines applicable to biological resource centres (BRCs) holding human-derived materials. The best practice guidelines cover the range of operations of such BRCs, including confidentiality and ethical issues, conditioning, conservation, distribution and/or transfer of human-derived material and the intellectual property issues. Insofar as possible, they follow the structure of the *General Best Practice Guidelines for all BRCs*.

These best practice guidelines should assist BRCs to put into practice procedures that comply with relevant national laws and regulations. The best practice guidelines aim to provide a reliable basis for research and development in different laboratories and to contribute towards protection of donors (as defined in best practices) in accordance with ethical principles, the health of laboratory personnel, the public and the environment.

4.5. Best Practices Guidelines for Animal and Plant BRCs

The BRC Task Force recognised that best practices should also be developed for those BRCs monitoring and supplying animal and plant-derived materials.

However, for a number of reasons, including the various other initiatives under way over the period that the Task Force sat, OECD member country experts decided not to take further action on developing such best practice guidelines at this point.

However, the Task Force was firmly of the view that such best practices should be developed in the near future perhaps under the auspices of any future global BRC network.

5. Implementation of Best Practice Guidelines

Each and every collection of biological resources (regardless of its profile and current status) is capable of improving its management of the issues referred in to in the attached sets of best practices. It is with this perspective that the Task Force considered the implementation of the best practices. Needless to say, optimal best practice would be achieved when all collections of biological resources fully comply with all the relevant areas of best practice set out in Part II.

However, from the perspective of an efficient functioning global network of BRCs (to be addressed in a subsequent report) that might comprise a range of different type and sizes of institution (from a national reference collection to a small, specialist academic collection) full compliance with all aspects of best practices might be neither necessary nor desirable, nor, indeed, possible.

Thus, though the full implementation of the best practices might be an ultimate goal for collections, it needs to be recognised that such implementation is a step-wise process which may need to be achieved over the longer-term for many existing collections.

Doubtless many collections would benefit from the experience of the larger, more developed BRCs in taking cost-effective steps to implement elements of best practice. Such “capacity-building” is just as useful for many collections in developed as in developing countries and should be a prime goal for a future global BRC network.

The OECD expert Task Force saw the responsibility for developing capacity, and climbing up the best practice ladder, as being shared between the collections themselves, the governments of the

states they are located in (especially where BRCs fulfil a role related to conserving *ex situ* biodiversity and/or materials required for the protection and maintenance of public health), and society at large. For practical purposes, however, it will be for the management teams of BRCs to decide and lay out what steps they will take towards achieving best practice.

The intention of the OECD effort, since its inception, has been to develop best practices which are sufficiently supported by the scientific community so that achievement of compliance with all relevant best practices is recognised as an achievement of quality management.

Some BRCs may wish to have such an achievement – *i.e.* complying with all the best practices set out in Part II – recognised and, indeed publicised.

Such recognition (or, indeed, recognition that certain rather than all aspects of best practices were complied with) could take a number of forms and would require some form of monitoring and assessment. Broadly, three different forms (first-party, second-party and third-party) of audit are available, though they are not mutually exclusive.

5.1. First-party assessment (self-audit)

Such an assessment would be carried out by the BRC itself. It results in a written confirmation known as the supplier's declaration of conformity. Self-assessment can be beneficial for a BRC given that it allows identification of gaps in quality management at different levels of a collection (technical, training, management, *etc.*). The outputs of the self-assessment can serve as the basis for developing a capacity building programme which provides the means by which a culture collection can successfully implement the best practices for BRCs. Such self-assessments are envisaged in the best practice guidelines as the means by which BRCs might carry out internal audits of quality management procedures.

5.2. Second-party assessment

Conformity assessment is carried out by a customer of the supplier organisation. For example, the supplier (BRC) invites a potential customer to verify that the products it offers conform to relevant standards or best practices. Such an approach might be adopted by a group of BRCs. Thus, a group of BRCs could establish assessment groups to assess their needs to move their quality management towards compliance with BRC best practice guidelines. In the same manner, such groups can set up training courses aiming to achieve full compliance with the best practice guidelines. Such an approach would lead to the transparency of activities among partners and to coordinated capacity building.

5.3. Third-party independent assessment (certification)

Third-party assessment is the preferred means by which conformity with specific requirements for a product (including service), system, process or material is assured in writing. The most well known such system is the ISO 9001 certification of quality management systems. Those that participated in the BRC Pilot Project designed to test and validate the best practices (see Chapter III, section 3) were of the view that a certification system based on an integrated quality management system such as ISO 9001 could be useful. Whether any such certification system should be established would, of course, be a matter for individual countries and/or BRCs to consider. Nevertheless, given the apparent interest, a possible approach for national certification of BRCs is provided in Part II of this report.

The expert Task Force recognised that implementation of the best practices is a prerequisite for quality improvement and should be monitored and reviewed periodically. The OECD could usefully give some further consideration to how such monitoring and review might be carried out – at least in the initial stages after adoption of the best practices – but in the medium to long term any such role should usefully be played by a global BRC network.

6. Adaptation for scientific and technical progress

The expert Task Force saw the best practice guidelines as "living" documents, which would need to be reviewed periodically and adapted to reflect scientific, technical and management progress.

The Task Force considered that such review would be a matter for BRCs to consider collectively, most likely through a future global BRC network.

7. Estimated cost related to implementation of best practice guidelines for BRCs

Implementation of the BRC best practice guidelines is associated with additional costs which are likely to have to be covered by BRCs. The costs associated with implementation of the OECD best practice guidelines can broadly be divided into three:

i) Costs associated with implementation of the OECD best practice guidelines by collections in their in-house procedures to achieve best practice in quality management. Such costs vary among the countries and depend on the actual status of the quality management of a given culture collection as well as on whether collections seek to implement best practices fully or partially.

ii) Costs associated with collections each going through the direct costs of third party assessment and compliance with best practice guidelines. Estimates here vary, but consultancy costs associated with pre-audit and certification for ISO standards run around EUR 30-50k. On top of this is the cost of any fee charged by the auditing agency. Depending on jurisdiction, a dedicated quality manager will cost a similar amount annually. One-off costs associated with technical compliance are too broad ranging to estimate and are highly dependent on local costs and on the original status of collections.[7] Recovery of these costs may be achieved through new business secured, but this is not guaranteed. Failure to achieve quality guidelines may of course mean the demise of a collection so a proper economic analysis would have to, for example, include potential exit costs.

iii) Costs associated with the establishment of any certification scheme.

Various indicative assessments of costs associated with compliance with the OECD best practice guidelines is given in Appendix III.

8. Building Capacity

The expert Task Force considered issues related to capacity building in some depth (for example, workshops were held in Africa and in Asia). The conclusions and recommendations of the Task Force will be included in the third OECD BRC report on the global BRC Network, expected in 2008.

7. UK collection managers estimate costs between around EUR 100 000 and EUR 340 000.

CHAPTER IV – SUMMARY OF RECOMMENDATIONS

The OECD Task Force on Biological Resource Centres endorses the best practice guidelines set out in Part II of this report (hereinafter "here") and recommends that:

i) The member countries of the OECD take steps to encourage the dissemination of these best practice guidelines and implementation of best practices amongst the potential user community;

ii) The user community itself (including, but not only, through the World Federation of Culture Collections) should not wait for government action but should immediately consider how to move towards implementation of the best practices set out here;

iii) Any entities subsequently taking steps towards developing a system of certification of compliance with the guidelines on best practice set out here should take due account of the considerations for national certification provided in Part II of this report;

iv) Implementation of the best practices, including the impact of such implementation, should be reviewed periodically;

v) The best practice guidelines set out here represent the current state of the art for best practice, but should be monitored and kept under periodic review so that they can be updated to take account of scientific, technological and management advances;

vi) The OECD might consider taking the first steps towards considering how such reviews should be carried out, but in the medium to long term it is recommended that a global biological resource centre network (hereinafter "GBRCN") should, if established, oversee these tasks;

vii) The user community should work together to address how capacity building to improve appropriate compliance with best practices should be organised and delivered. If a GBRCN is established consideration should be given to the network overseeing this process;

viii) The user community should work together to develop further information linkage and exchange systems between BRCs, possibly under the auspices of a GBRCN;

ix) The user community should work together to develop sustainable financing strategies for BRCs, possibly under the auspices of a GBRCN;

x) OECD member countries, together with partner non-member countries, should take additional steps to develop a virtual, inclusive GBRCN based on the recommendations above and a commitment to work towards quality improvement.

These recommendations, and the best practice guidelines to which they refer, were endorsed by the OECD Working Party on Biotechnology at its 21st session on 19-21 February 2007 and by the OECD Committee on Scientific and Technological Policy at its 89th Session on 26-27 March 2007, both in Paris.

Part II

BEST PRACTICES

FOREWORD

These guidelines provide the basis for best practice in the management of Biological Resource Centres maintaining replicable biological materials. It draws together the key principles and best practice of quality management systems and operational guidelines prescribed by individual national public service collections and national, regional and world culture collection organisations. The initial input was provided from the Common Access to Biological Resources and Information (CABRI) Guidelines and the UK National Culture Collection (UKNCC) Quality Management System. It has been adapted to meet the needs of the user community.

This document provides specific best practice guidelines on the operation of Biological Resource Centres (BRCs) as defined by the OECD (2001) *Biological Resource Centres: Underpinning the Future of Life Science and Biotechnology* to assist in establishing general best practices for managing BRCs.

Guidance for the operation of Biological Resource Centres (BRCs) comprises several sets of best practice guidelines that together provide the basis for best practices in the management of BRCs. Two sets of general best practice guidelines address all Biological Resource Centres, no matter what type of biological material they hold and supply. These are: *General Best Practice Guidelines for all BRCs* and it is supplemented by and *Best Practice Guidelines on Biosecurity for BRCs*. Further best practice guidelines provide additional best practices for those BRCs that hold and supply biological material within specific domains. Best practice is achieved when BRCs comply with all sets of general best practice guidelines applicable to the specific domain that the biological materials they hold and supply belong to. Currently two sets of such OECD best practice guidelines exist; *Best Practice Guidelines for the Micro-Organism Domain*, and *Best Practice Guidelines for Human-Derived Material*. Further domain-specific best practice guidelines for animal and for plant material are regarded as necessary, and might be developed under the auspices of a future global BRC network.

Where elements addressed in best practices are covered by existing national and/or local laws and regulations, such laws and regulation must take precedence.

GENERAL BEST PRACTICE GUIDELINES FOR ALL BRCS

1. Introduction

Living organisms, their cells or their replicable parts (*e.g.* genomes, plasmids, viruses, cDNAs,) are the basic elements of the life sciences and biotechnology. They are utilised in large numbers as living reference materials for testing, identification, the production of compounds, fuel and food. They are the tools for knowledge generation and biodiversity conservation. They are grown, maintained and utilised around the world and are key to many research programmes, industrial processes and training courses. These biological resources should be maintained without change to ensure reproducibility and sustainability.

Collections of biological materials range from small private centres through to large service centres, and have widely differing objectives, policies and holdings. They are often linked to activities of the parental organisation, for example, teaching or life sciences research, and the organisms they hold may have many different uses. Collections of data (databases) hold data that is directly linked to biological materials held in a Biological Resource Centre (BRC).

It should be the policy of BRCs to provide their users on every legitimate occasion with the products and services they require. These products and services should be of consistently high quality and fulfil product claims as defined in their catalogues. At all times appropriate techniques and procedures that comply with relevant national law, regulations and policies should be in operation. Regular audits should be carried out to ensure that these procedures are followed and are effective.

In order to achieve best practice in the acquisition, maintenance and provision of biological materials the best practice guidelines given in this document should be followed.

2. Scope

These best practice guidelines give general best practice for the acquisition, maintenance and provision of biological materials and on the management of Biological Resource Centres as defined by the OECD (see definition below, section 3(ii)).

The purpose of these best practice guidelines is to help ensure that biological materials are of the highest standard and authentic. The preservation techniques used should retain the key features of the biological material and ensure its consistency between centres supplying it. This will help to provide a reliable basis for research and development in different laboratories and to contribute towards protection of the health of laboratory personnel, the public and the environment.

3. Definitions

(i) Biological materials

The term 'Biological material' as used in this document covers all materials listed in the Organisation for Economic Co-operation and Development (OECD) definition of BRCs given below.

(ii) OECD Definition of Biological Resource Centres (BRCs)

"Biological Resource Centres are an essential part of the infrastructure underpinning biotechnology. They consist of service providers and repositories of the living cells, genomes of organisms, 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 data bases containing molecular, physiological and structural information relevant to these collections and related bioinformatics. BRC 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."

(iii) Authentication

Authentication is the process by which biological materials are characterised up to a defined level using appropriate technology to establish a conclusive basis for accepting the material as genuine. This process is defined in the domain specific best practice guidelines for BRCs.

4. Organisational requirements

The BRC should meet the OECD definition and must be compliant with appropriate national law and regulations. A BRC should describe and document the nature of the biological resources it holds. It should define the biological domain and therefore the domain specific criteria that apply, *e.g*. micro-organisms or human-derived materials.

4.1. Long-term sustainability

The BRC should develop a strategy for its long-term sustainability. Adequate and reliable sources of funding vary from government support, income from services and private support.

If its future is threatened**,** the BRC should have a plan to ensure that its key holdings remain available.

4.2. Responsibilities of management

Primary responsibility lies with the BRC senior management who may delegate responsibility for implementation of its policies to named and suitably qualified members of staff and provide them with defined responsibilities and authority. The list of such staff and their specific responsibilities should be available to all staff of the BRC and should particularly be made available to new staff, students and visitors.

The Senior Management of each individual BRC should ensure that appropriate resources are available for staff members to discharge its responsibility towards this policy. The BRC should appoint a Quality Manager whose duties include:

- Administering and monitoring an efficient up-to-date quality management system.
- Reporting and advising on quality matters.
- Representing the BRC on quality matters when dealing with users, suppliers and outside bodies.

Where possible a deputy should be appointed to serve in the absence of the quality manager. The Quality Manager has direct access to the Senior Management of the BRC on matters concerning quality.

BRC should designate a biosecurity officer, at operational level within the BRC, whose responsibility it is to ensure internal compliance with *Best Practice Guidelines on Biosecurity for BRCs*.

4.3. Staff - qualifications and training

Staff may be engaged at many levels of experience and qualifications but they should not be allocated to any piece of work without expert training, or until training appropriate to the job is completed and they are proved competent. Each member of staff should have documented job descriptions with specific delegated tasks and defined responsibilities.

Staff should be trained according to documented protocols in skills specific to the job and should receive training as new technologies or practices are introduced. Such training should be reviewed annually. All BRC staff has a responsibility towards the main objective of a BRC that is to provide high quality, biological resource services to the public.

Authorisation to use specialist equipment should be documented in training records. For example new staff should not be allowed to use autoclaves, centrifuges, freeze-drying equipment, cryopreservation facilities, safety cabinets until they have been trained in their use and are proved competent.

All staff involved in providing a product or service contribute to the achieved quality. The role of the quality management system is to guide and advise staff on quality matters and to provide independent assurance of quality to the Senior Management.

It is the responsibility of all staff to familiarise themselves with documented protocols and comply with the policies and procedures laid down in the BRC Standard Operating Procedures and associated documentation at all times. It is the management's responsibility to ensure that staff has access to Quality Manuals and that they are understood and kept informed of any amendments.

4.4. Health and safety (biosafety)

All staff should follow the procedures laid down under the appropriate level of containment for the organisms being handled to avoid contaminating samples and risk of infection (details are provided in the Domain Specific Best Practice Guidelines for BRCs).

5. Premises

An environment should be provided that is conducive to handling authenticated materials appropriate to the organism domain and to facilitate the acquisition, maintenance and provision of biological materials and its services.

It is the responsibility of the member of staff allocated to a task to check that the accommodation is clean and well lit and that usual aseptic techniques are followed. Appropriate protective clothing should be worn and safety procedures followed.

Appropriate arrangements, in accordance with national and international regulations, for site security should be made to ensure hazardous organisms cannot be released to unauthorised users.

The BRC should describe the premises and processes (including all areas under the responsibility of the BRC) used for the specific operation of the BRC. These areas, as well as the environment and equipment in the premises, should be in conformity with all relevant national and international standards and regulations.

The safe operational level or safety limit for the resources available should be justified and documented and the BRC should not operate beyond these limits.

5.1. Biological Resource Centre operations

Appropriate areas are required for the specific operation of a BRC as appropriate to the domain of the biological materials. The activities that should be accommodated are as follows:

- Receipt and storage of the initial sample.
- Preparation, regeneration, handling and processing of samples.
- Biological material storage area and back-up or safety duplicate collection. Duplicate collection should be preferably in a remote building or alternative site.
- Supply, delivery/sales (kept separate from incoming accessions).
- Decontamination and cleaning of equipment and processing of wastes.

There are several ways to achieve the above as an alternative to having separate areas. For example: *(a)* to construct the laboratory on the 'no way back' principle, *(b)* to carry out procedures in a sequential manner using appropriate precautions to ensure sample integrity (*e.g.* use of sealed containers), *(c)* to segregate activities by time and space.

Other areas associated with the BRC should be structurally sound, unobstructed, clean and free from laboratory materials.

5.2. Construction and operation

Construction should meet appropriate national regulations and policies *e.g.* to the containment level appropriate for the risk (hazard) group of the organisms worked with. If major building, renovation, repair or dirty work is necessary in BRC laboratories, normal activities should be suspended until the building, renovation, repair or dirty work is completed.

5.3. Access

The minimal requirement is to restrict access to the BRC to authorised staff or those accompanied by them. BRCs housing hazardous biological materials should pay particular attention to security and where appropriate be fitted with security devices (see *Best Practice Guidelines on Biosecurity for BRCs*).

5.4. Maintenance and inspection

Cleaning and decontamination procedures should be documented. Buildings should be cleaned on a regular basis. Cleaning of organism containment areas and specialist equipment should be performed by authorised and trained staff using appropriate personal protection equipment following documented procedures.

5.5. Outside support services and supplies

Any support services used by the BRC should be of adequate quality to sustain confidence in its activities. Supplies should be sought from reputable companies with, where possible, proven quality of products. Preference should be given to services and supplies covered by certification schemes. Where no independent assurance of quality of support services is available, the BRC should be responsible for confirming the quality of vital supplies. Copies of purchase orders

should be held on file and records of suppliers, standing orders etc. should be maintained for a minimum period of five years.

6. Equipment use, calibration, testing and maintenance records

Equipment management procedures including use, control of performance, maintenance and calibration should be laid down in a predefined schedule. Instructions for these activities should be laid down in the manufacturer's handbooks/manuals or in the BRC procedure. Service records should be maintained and copies of key documents should be held in the BRC Equipment Maintenance and Calibration Log books in the care of the Quality Manager.

7. Documentation management

The BRC Quality Manager should be responsible for ensuring that all documentation is correctly updated. Alterations to any operating documents should not be allowed unless agreed to by the Quality Manager. Amendment sheets should be issued to all holders. Short-term sanctioned alterations should be made in ink by scoring through existing wording so that it is still legible – scribble, correction fluid or tape should not be allowed. The alterations should be signed and dated by the Quality Manager. Copies of the quality manual and, if appropriate, specific procedures should be such that they can be made available to enquirers, course participants and staff through the BRC Quality Manager. In such cases, they should be provided with copies clearly marked as uncontrolled copies and such copies should not be updated.

7.1. Compliance with internal documentation

All staff should adhere to the prescribed policies and procedures. Any departures from documented procedures should be agreed by senior management prior to deviation. Written permission and justification should then be included in the relevant records.

In the case where a procedure is not followed a deviation report is required outlining the specific error and corrective actions that will be taken. If failure has been brought about by a misunderstanding or misdirection, the error should be investigated, rectified and retraining implemented if necessary.

8. Data and informatics

The BRC should manage and store data and produce electronic catalogues based on authenticated and validated information.

8.1. Data management

Depositors are responsible for assuring the quality of data associated with the biological material. The BRC may require evidence to assure the validity of the data.

The authentication of data may differ from centre to centre, but a BRC should:

- Provide traceability of data through a history of modifications (dates and signatures of inputs, validations, modifications and deletions).

- Give signature for data entry, validation, modification or deletion.

The BRC should use a standard terminology and formats for data management and exchange and standard protocols for data transmission to networks (domain, regional or global networks):

1. Select data format, data representation and data transportation taking into consideration existing standards for data processing, *e.g*. DarwinCore/DiGIR and ABCD schema/BioCASE for strain data, CCINFO for the organizational information of BRCs.

2. Check vocabulary against standard reference lists or thesauri.

3. Keep consistency among BRCs for searching and retrieving of information from catalogues and databases:

- Each biological material record should contain a Minimum Data Set, a Recommended Data Set and/or a Full Data Set in accordance with domain specific criteria.

- Spell checking for every field should be a basic requirement.

- International English should be chosen as a preferred language of data (in addition to local language if different).

- A standardised approach should be adopted to certain scientific symbols (to avoid any errors due to incorrect reading of a character set, standard ASCII alternatives to symbols should be used: *e.g*. Greek letters cannot be used, they should be fully spelled (write alpha, gamma, beta…); the °symbol for temperature is to be omitted entirely (*e.g*. 37C replaces 37°C); no subscripts or superscripts are allowed (*e.g*. cm3 replaces cm^3 and CO_2 replaces CO_2).

BRCs should adopt procedures to detect errors in data to improve their quality and consistency. This is an essential part of information management and should be both applied to the input of new data as well as to pre-existing information in current databases:

- For existing data, a series of checks should be carried out to ascertain their validity and completeness. As more BRCs become associated, more searches should be made for common classes of error to allow more efficient error correction.

- For new data, wherever possible, inputting should be checked against authorised lists of not only scientific names but also thesaurus/ontology to prevent errors such as mistyping.

- BRCs should present evidence that they have applied a recognised protocol appropriate for each data element.[8]

8 . A comprehensive treatment of Data Cleaning can be found in Chapman, A.D., *Principles and Methods of Data Cleaning – Primary Species and Species-Occurrence Data,* Version 1.0, Publisher - Global Biodiversity Information Facility (GBIF), 2005.

8.2. Data processing

The informatics system employed by BRCs should provide appropriate facilities for information management, linkage and exchange of the BRC.

The databases should contain either information relating to strains held by a BRC (which at least, should be retained as long as a strain remains viable), or other relevant data items or composite data needed by the BRC (*e.g.* users records). On the loss of a strain the database record should be either printed and stored on file or copied to a digital archive before the entry is removed from the working database, placed in reserve or annotated to indicate that it is no longer available as living material.

The BRC should preferably choose standard data schema and protocols to make the databases distributed and interoperable. Confidential data should be clearly identified in relation with user authentication capability, encryption techniques and other related information security tools.

The informatics system should ensure regular data back-up. Off-site storage of data is desirable. Data archives should be maintained in accordance with the maintenance of the biological resource storage policy. The support of these archives should be regularly updated according to its physical characteristics (obsolescence) and to software compatibility.

BRCs should introduce appropriate measures (protocols, tools and standards) in their own informatics systems to assure reasonable security of information. There are existing systems, *e.g.* authentication by user ID and password, encryption, encryption of messages and restriction of IP addresses that may provide the basis for such measures. Backup-files should be stored in secure cabinets.

8.3. Access to data and publication

The BRC should make available data describing the biological material and its origin and provide electronic catalogues to users through their own facilities (*e.g.* website) or through focused, national, regional or global networks. Data should also be retained for traceability in compliance with relevant national laws and regulations.

The BRC should respect a defined update frequency for data publication (on-line or not), in accordance with the flow of available biological resources.

BRCs should ensure the quality and consistency of data sets and provide data to users while ensuring information security, bio-security, protection of IPRs, client information and human dignity. National data protection regulations shall be adhered to.

Exchange of information should be in line with the OECD Guidelines on the Protection of Privacy and Transborder Flows of Personal data.

BRCs should restrict access to the electronic catalogues where appropriate.

Users should be authenticated. Specific identities and passwords should be provided by BRCs to users to access different categories of information and services. The validity of identifiers and passwords should be checked.

9. Preparation of media and reagents

The BRC should define standards for all preparations used in the growth and/or maintenance of the living biological materials held; these should be documented with the appropriate mechanisms in place to allow changes to procedures.

Supplies of materials for use should be of high standard and should not be contaminated.

10. Accession of deposits to the BRC

10.1. Receipt and handling of biological materials

The BRC should document and implement procedures for the receipt and storage appropriate to the type of biological materials handled.

A risk assessment should be carried out on the biological material and the methods recorded to determine, as far as possible, the potential of harm to personnel, the public and the environment. The risk assessment should be reviewed and updated regularly.

A unique collection number is allocated to the biological material, which is never reassigned if the biological material is later discarded.

10.2. Accession

The BRC should document its acquisition policy defining the biological material to be maintained and the criteria on which the acceptance of new biological material offered to the collection is based. This policy should balance capability, capacity with scientific and user's needs.

BRCs should only accept deposits of biological material that meet its acquisition criteria and fall into the groups of its specialist expertise.

The biological material received should have the following information:

a) Name (where one can be applied), other identifier or cell culture description.

b) Depositor's name and address.

c) Source, substrate or host from which the biological material was isolated or derived (where identified) and date of isolation.

d) Geographical origin of material (the minimum requirement is the country of origin or the furnisher of the source, substrate or host).

e) Depositor's biological material number or other collection number(s), if deposited elsewhere.

f) Growth media and conditions, cell preservation or storage conditions where known.

g) Hazard information *e.g.* in the form of a safety data sheet.

10.3. Quality checks on the biological material

The BRC should perform authentication tests as well as determine the stability of some key features, growth requirements, and methods of maintenance and/or preservation as appropriate to the biological material maintained, using appropriate technology. This information should be

recorded. These records should be retained and can be used as a base line when in-storage maintenance checks are performed or for validation after preservation restocking.

Where possible the identity of the biological material should be confirmed after receipt by a competent person (employed or contracted by the BRC or its parental organisation). The biological material should be checked again by these competent persons before (if there are additional transfers of the biological material before it is preserved) and after preservation. This step may include identity, purity or property check of the biological material performed by the depositor.

A "maintenance plan" (*i.e.* a scheme for periodic control of the preserved material) should be in place for each item stored. Several aspects determine the frequency of the maintenance checks (*e.g.* the type of biological material, the preservation method, turnover of the material, etc.). The maintenance check should be appropriate to the biological material and be laid down in the domain specific criteria.

See domain specific recommendations for specific details of quality controls.

11. Preservation and maintenance

The BRC should select preservation and maintenance methods according to recommendations from the depositor and/or previous experience. The BRC should document these preservation procedures to ensure they are reproducible and that key parameters of the process are recorded and monitored.

11.1. Methodology

The biological material should be preserved by at least two methods (where two distinct methods are not applicable to the biological material, cryopreserved stocks should be maintained in separate locations) and as master cell banks and as stocks for distribution. The details of the preservation techniques are laid down in the domain specific criteria.

The labels should include at least the batch date or number and the BRC accession number. Where possible an indication of expiry date should be provided to the user of the biological material. Biological materials with specific hazards should be clearly differentiated.

11.2. Stock control of the preserved biological materials

To ensure a minimum number of transfers or generations from the original biological material, where this is appropriate, the BRC should use master (or seed) and distribution stocks.

The BRC should produce the master stock from the original biological material. This master stock should be used to generate the distribution stock. The BRC should use the distribution stock to supply biological materials.

The BRC should adapt the size of these masters and distribution stocks to the anticipated distribution rate.

11.3. Storage of preserved biological materials

The biological material should be stored under environmental parameters that assure the stability of its properties (see domain specific obligations).

Details of the inventory control, lead times and re-stocking practices should be documented.

A duplicate collection should be maintained, preferably on another site as a 'disaster' protection measure and to avoid accidental loss.

11.4. Validation of methods and procedures

The BRC should document all methods and procedures used in validation (see domain specific criteria).

The results of method and procedure validation should be recorded.

12. Supply

12.1. Order placement

The BRC should only supply to users who have the appropriate facilities and meet the specific requirements for receipt as required by relevant national and international regulations and policies.

The materials should be distributed according to the policy of each depository. This policy should take into account the nature of the biological materials and meet all relevant national and international regulations and policies.

An order should only be accepted when the required accompanying documentation is completed, signed and returned.

12.2. Availability of the biological material ordered

If a biological material cannot be delivered within the specified delivery time, the BRC should contact the user with an estimated supply date. The BRC should recommend where possible other national or foreign BRCs to supply biological materials not held.

12.3. Information provided with the biological material supplied

The BRC should provide at least the following information to the user:

- Biological material identifier, accession number and batch number.
- An estimate of shelf-life, storage conditions, storage instructions and if appropriate, conditions of growth.
- Instructions for opening ampoules or vials (when appropriate and in all cases where materials are being provided to new users).
- A safety data sheet including the containment level required for handling the biological material, disposal measures and measures to take in case of spillage.
- A Material Transfer Agreement: an essential requirement to protect IPR and mandatory where they are required by national law. They are used to relay the depositor's and/or country of origin requirements on use of the biological material.[9]
- Fax-back sheet to acknowledge receipt of materials may be desirable.

9. Examples of MTA content can be found as an annex to the Bonn Guidelines (http://www.biodiv.org) and as an output of the MOSAICC project (http://www.belspo.be/bccm/mosaicc) - both voluntary codes of practice.

12.4. Packaging

The BRC should pack and send its biological material according to current postal, IATA and ADR regulations. It should also meet additional requirements imposed by other regulations such as quarantine, biosafety and/or biosecurity regulations.

12.5. Invoicing for supply charges

Invoices should normally be despatched at the same time as the material unless otherwise instructed or where *pro forma* invoices have been paid in advance.

12.6. Traceability of biological materials supplied

The BRC should keep records of all requests for biological materials – including those requests refused for any reason – showing the biological material, method and date of shipment, and name and address of the person to whom sent. Where recorded delivery, courier or similar shipping mechanisms are used records of shipment receipt should be maintained. The records should be maintained to meet national law, regulations and policies.

12.7. Handling complaints and anomalies

The BRC should record all user queries or complaints and acknowledge as soon as possible (preferably on the same day) by fax, telephone or e-mail.

The BRC should investigate the complaints as soon as received and implement the necessary corrective actions. All complaints should be included in regular trend analysis.

Records of responses/solutions should be stored.

12.8. Refunds

Despite rigorous quality control and standard procedures being followed, it may be possible that the biological material provided may not have the property stipulated in the order or that is reasonably expected of it on receipt. If the user is not deemed at fault it is normal policy to provide the user with a replacement free of charge where this is possible. If refunds are considered appropriate they should be given.

12.9. Confidentiality

All work carried out for a client should be treated as strictly confidential to that client unless national requirements apply. This should apply to all requests for biological materials, safe and patent deposits, information supplied relating to these and to the fact that the product or service was requested in accordance with national law, regulations and policies. Information may be included in statistics produced to show BRC activities in a way that the customer is not identified.

The names of past or present clients should only be revealed with the clear permission of the client.

13. Quality audit and quality review

13.1. Purpose

Periodic audits should be carried out by management to ensure that the BRC policies and procedures, as set out in these best practice guidelines and the supplemental domain specific best

practice guidelines, are being followed. External, independent audits should be carried out. A process should be in place to identify any potential source of non-conformity to BRC guidance.

13.2. Responsibility

The BRC manager or a delegate, assisted by BRC staff if necessary, should carry out an assessment of the effectiveness of procedures and organise the audit programme.

The Quality Manager should be responsible for ensuring that reviews are recorded and that any actions are implemented.

13.3. Implementation

Staff of the BRC should undertake at least one audit each year according to the schedule described in the Rolling Audit Programme. This programme entails the review of all BRC activities including documentation, supply, accession, database, training records, equipment and maintenance, enquiries and complaints records and external support services. In addition it should include a strain deposit trail through to storage and a supply trail from receipt of order to supply. These should be chosen at random. The Day Work Books, enquiry records and database records should also be reviewed. The results of the audit and record reviews should be recorded and any fault rectified.

An external independent qualified person should carry out a Third-Party Audit of the procedures, preferably each year. This too should include a biological material deposit trail through to storage and a supply trail from receipt of order to supply. These should be chosen at random. The Day Work Books, enquiry records and database records should also be reviewed. The results of the Third-Party Audit and record reviews should be recorded and any fault rectified.

A meeting of all audit staff, BRC staff and line management should be held annually to review the audit reports, enquiries and complaints received and discuss potential improvement in procedures and monitoring. The results of the review should be recorded and the Quality Manager is responsible for implementation of actions prescribed.

13.4. Method and procedure for quality checks

All methods and procedures should be subject to in-use quality checks. For example, the product should be checked for fitness for purpose, *i.e.* a sample should be selected from a preserved batch and appropriate stability checks carried out. Such checks should be included in the individual documented procedures.

BEST PRACTICE GUIDELINES ON BIOSECURITY FOR BRCS

Introduction

Biological resources underpin all biological sciences research. They provide the source material for scientific investigation, leading to many of the discoveries on which biotechnology is founded. Providing for high quality maintenance and rapid low-cost exchange of biological resources and quality information on them is a key issue for efficient advancement of the biological sciences. Quality assurance and protocols followed by Biological Resource Centres (BRCs) meet this need.

BRCs espouse openness of information and the ability to exchange material quickly; they therefore need to provide certain safeguards that such material and information will not be misused for nefarious purposes. The prospect of bioterrorism generates the need to secure facilities that work with, store or transfer dangerous biological material to ensure that such materials are not susceptible to misuse for malevolent ends. Thus, to contribute most effectively to scientific and economic development, BRCs should not only promote scientific openness but also a sense of security. The two goals are equally important and should be balanced and should be mutually reinforcing.

To deliver such a balanced and mutually reinforcing effect the aim of biosecurity best practice guidelines for BRCs is to reduce the probability that dangerous biological material could be obtained by unauthorised persons and deployed to cause harm, without unduly hindering research or being financially burdensome. Such best practice guidelines should be clearly articulated and grounded in an understanding of the biological material and the operations of BRCs.

1. General Provisions

The biosecurity best practice guidelines stated herein provide a basis for establishing best practices to secure the maintenance and provision of biological materials held by BRCs. They are designed to be implemented in conjunction with the general operational guidelines for all BRCs and the applicable specific domain best practices for BRCs.

BRCs should implement these biosecurity best practice guidelines in a manner that does not conflict with obligations under national, local and/or international laws and regulations.

2. Scope

These biosecurity best practice guidelines are designed to apply to BRCs. They propose a framework for risk assessment of materials held within a BRC as well as a framework that sets out best practices for management of such risk.

The frameworks for risk assessment and risk management contained herein provide tangible tools for biosecurity. These are necessary but not sufficient to ensure biosecurity, however. Just as important will be a demonstrable culture of responsibility and awareness of security throughout a BRC. The assignment of an individual within a BRC who has, as part of his/ her responsibilities, the general oversight of procedures within a BRC to ensure biosecurity is essential to achieve best practice and will contribute towards the said culture of security. The management and staff of a BRC should also share a sense of responsibility for biosecurity and a BRC should be able to demonstrate that this is the case.

3. Definitions

The definitions in *General Best Practice Guidelines for all BRCs* apply with the additions below.

- "Biosecurity": Institutional and personal security measures and procedures designed to prevent the loss, theft, misuse, diversion or intentional release of pathogens, or parts of them, and toxin-producing organisms, as well as such toxins that are held, transferred and/or supplied by BRCs**.**

- "Risk assessment": The process of identifying sources of potential harm associated with the loss, theft, misuse, diversion or intentional release of pathogens, or parts of them, and toxin-producing organisms, as well as such toxins that are held, transferred and/or supplied by BRCs, assessing the likelihood that such harm will occur and the consequences if that harm occurs

- "Risk management": The process of weighing policy alternatives, considering risk assessment and other factors relevant for biosecurity, and selecting appropriate prevention and control actions**.**

- "Security breach": A security breach is any violation of the biosecurity best practice guidelines where these are intended to be in place as best practices.

- "Risk communication": The interactive exchange of information and opinions among personnel of the BRC and, where appropriate, other parties, concerning risk-related factors and risk perceptions.

4. Assessing biosecurity risks of biological material

BRCs should ensure that a detailed inventory of the different biological materials they hold is available.

BRCs should conduct a risk assessment of the biological materials in their inventories for the purpose of assigning such materials to biosecurity risk levels, which may be assigned as high, moderate, low or negligible (see Table 1). The level of biosecurity risk of biological material should be determined according to the best available information on its potential for malicious misuse (including economic consequences) as well as its virulence**.** Risk assessment should address the potential of biological materials, should they be obtained and misused by unauthorised persons, to cause harm to the health of humans, crops, livestock or infrastructure.

The provision of biosecurity should be regarded as a benefit to society at large. The burden of risk analysis should thus be shared collectively by BRCs and the broader science policy community. BRCs should engage in and together develop expert networks that can contribute to the provision of risk analysis.

BRCs should share their experience with other BRCs as regards the results of qualitative risk assessment and the reasons for assigning the biosecurity risk level of a particular biological material, and make all such documentation available to competent national authorities.

BRCs should determine a biological material's biosecurity risk level as a function of its potential for malicious misuse and its virulence. Establishing the biosecurity risk level of a particular material is instrumental to applying the Biosecurity Risk Management Practices in Section 6 below.

BRCs should assess potential for malicious misuse based on the following key factors:

- Availability: the number of facilities that stock the biological material and their geographical distribution.

- Amplification: the ease with which the biological material can be replicated, for example whether it can be grown in culture and its growth rate.

- Skills and knowledge: the ubiquity or rarity of the skills and knowledge necessary to amplify and/or genetically modify the biological material.

- Dispersal: the ease and effectiveness with which the biological material can be dispersed, such as by air, water, food or by other means into the environment. This might include (but not be limited to) a biological material's aerosolisation and inhalation characteristics.

- Environmental viability: the hardiness of the biological material across a range of temperatures, humidity levels, light exposures.

- Countermeasures: the existence of and ease of access to prophylaxis, post-exposure treatments and detection and decontamination measures.

- Economic consequence: the extent to which the biological material may be used to bring about harmful economic consequences for humans, crops, livestock or infrastructure.

BRCs should assess virulence based on the following key factors:

- Infective dose: the smallest quantity of the biological material necessary to cause infection.

- Pathogenicity: the disease-causing ability of the biological material.

- Lethality: the ability of the biological material to cause death to the host.

- Transmissibility: the ease with which the biological material can spread either by vector to host, or host to host.

In addition to the key risk factors set out above, other factors could materially affect the assessment of a biological material's potential for malicious misuse as well as its virulence. Where such factors are known it is the responsibility of the BRC to ensure that due account is taken of them in determining the overall biosecurity risk level of a biological material.

It is important to remember that in some cases, one risk factor may be so significant that it may determine the overall risk rating for a particular biological material. Thus, BRCs should carry out risk assessment in such a manner that risk factors are weighed.

In conducting risk assessment, if there is doubt as to whether a particular factor of a biological material should be characterised as high, moderate, low or negligible, BRCs should consider assigning that factor to the higher of the two possible levels. This need not imply that the overall biosecurity risk level for biological material is deemed higher.

BRCs, with the broader scientific community, should take steps, as a priority, to develop common methodologies for risk assessment and should seek to develop quantitative and qualitative tools

and assessments that assist in completing appropriate and comparable risk assessment. For example, they may conduct statistical analysis for the purpose of establishing average biosecurity risk levels for the same type of biological materials, and to signal conflicting biosecurity risk levels, in different BRCs. Reporting will also allow the establishment of a data base that BRCs may use as a reference. Such an approach will permit the harmonisation of data generation, and thus lead to an increasingly harmonized framework of risk assessment and risk management amongst BRCs. In developing common tools and methodologies, BRCs, with the broader scientific community, should be sure to draw on appropriate existing – including international – tools and methodologies. For example some list-based approaches currently used to assign risk may be deemed as useful inputs to risk assessment for the purpose of biosecurity.

5. New acquisitions/re-assessment of inventory

BRCs should make biosecurity risk assessment, as described in Section 4, part of the acquisition process of new biological material.

When being transferred between BRCs, a summary of a biological material's risk assessment should be made available to the recipient BRC. A new risk assessment should only be conducted if, after reviewing the summary, there appears to be new circumstances or information that affects the original assessment; in such case, the procedure for risk assessment set-out in Section 4 should be followed.

BRCs should re-assess the biosecurity risk level of materials for which there is new information about their virulence or potential for malicious misuse.

6. Biosecurity risk management practices

BRCs should implement the biosecurity management practices contained in sections 6.1-6.9 below in a graded manner to reflect the level of biosecurity risk of biological materials.

Risk management applies to biological material at all times, including the receipt, storage, use, transfer and disposal of materials.

BRCs should establish a timetable for internal audits to check for the level of compliance with the risk management practices. These evaluations should conform to the rolling audit and review programme as described in the document *General Best Practice Guidelines for all BRCs* Section 13.3.

BRCs should designate a biosecurity officer, at operational level within the BRC, whose responsibility it is to ensure internal compliance with the biosecurity best practice guidelines contained in this document.

6.1. Physical security of BRCs

BRCs should conduct all activities with biological material in an area that corresponds to the appropriate biosecurity risk level resulting from the application of the biosecurity risk assessment described in Section 4. A potential scheme of physical security levels is given in Table 1 below.

Table 1. Potential scheme of physical security applicable to biosecurity risk levels associated with the BRCs

Biosecurity risk level	Physical security
Negligible or Low	General security area
Moderate	Restricted area
High	High security area

BRCs should design (or adapt the design of existing construction of) their physical facility to reflect the requirements of sections 6.1.1-6.1.3 below. BRCs should supplement the general security area (6.1.1) by additional layers of physical security within the facility, if they possess biological material that presents a high or moderate biosecurity risk level. Biological material presenting a moderate biosecurity risk should be stored and worked with primarily in a restricted area (6.1.2), whereas biological material presenting a high biosecurity risk should be stored and worked with in a high security area (6.1.3).

6.1.1 General security area

BRCs should implement physical security measures that provide a general security barrier against theft and persons gaining unauthorised access to facilities and the material therein. The area enclosed by the general security barrier typically marks the physical boundary of the BRC. The general security barrier should be equipped with access controls, typically available to all staff at the facility. Access controls can be in the form of manual keys, electronic key-cards, presentation of staff ID badge to security guard etc. The general security area may or may not be equipped with a 24-hour intrusion detection system.

6.1.2 Restricted area

The restricted area is characterised by an additional layer of security and access controls through which only those staff authorised to have access to the materials held within may pass. Access to a restricted area requires an additional access item that is only available to individuals who are authorised to access the materials held within. The access item may be a manual key, key-card, electronic access code or a specific ID badge signalling that the individual has a different level of access than staff with access to the general security area only. Restricted areas should be enclosed on all sides within the general security area, *i.e.* the restricted area should not share a boundary with a public area. The restricted area should be equipped with a 24-hour intrusion detection system.

6.1.3 High security area

The high security area should be nested within a restricted area and should not under any circumstances share a physical boundary with the general security area. The high security area is characterised by an additional layer of security and access controls through which only those staff authorised to have access to the materials held within may pass. Access to the high security area requires an additional access item that is only available to individuals who are authorised to access the materials held within. The access item, key, key-card, electronic access code, specific ID badge should signal that the individual has a different level of access than staff with access to only the general or general and restricted areas. The high security area should be equipped with a 24-hour intrusion detection system.

The construction of restricted and high security areas should be such that any apertures (windows, ventilation shafts) that are sufficiently large for a person to gain entry through are secured to prevent this. Emergency exit doors should be releasable only from the inside, unless prevailing safety codes provide otherwise.

BRCs should maintain equipment/facility maintenance logs of the security areas, including names and affiliation of maintenance personnel.

6.2. Security management of personnel

The BRC manager should ensure that attentive management practices in the supervision of staff are the norm.

BRCs should institute security screening, in line with national privacy law, and set in place best practice guidelines describing how decisions on appointments (or granting existing staff a higher access level) should be taken according to the nature of the facts that emerge about the individual. Background checks of staff whose duties require them to have access to material that presents a high or moderate biosecurity risk should be conducted prior to the granting of access to such biological materials.

All staff should be issued with an identification token, preferably equipped with a photograph of its issued holder, and providing information as to their level of access. Identification tokens should be worn at all times except in circumstances where doing so would present a health and safety risk (when wearing a biohazard suit for example). Identification tokens should be surrendered upon termination of employment at the BRC. BRCs should keep records of current and former employees, while paying due respect to their privacy.

6.3. Security management of visitors

BRCs should establish a system of security controls for visitors.

A BRC's system of security controls should include a list of the types of visitors that it allows to enter its facility and classifies whether the visitor should be escorted or unescorted.

Unescorted visitors should be subject to the same security management procedures as BRC personnel (see section 6.2). Alternatively the facility may choose to accept the security clearance conferred on the visitor by a government agency, or other appropriate body, provided that security clearance is current.

In general, escorted visitors should not have access to restricted or high security areas.

BRCs should maintain visitor logs, ensure that visitors do not enter the facility with prohibited items, and issue visitors with a colour coded badge (or equivalent means) according to the level of biosecurity risk to which they have access. Badges should either automatically expire when the visitor leaves, or be taken from the visitor on exiting. Appropriate visitor-to-escort ratios should be established for different security areas (for tours within the general security area 10:1 or higher may be appropriate, whereas escorting maintenance staff within the high security area may require a 1:1 ratio).

Permission to visit the facility should be granted by the manager of the BRC or a designee. Decisions on visits to restricted and high security areas should be taken in consultation with the biosecurity officer (where such an individual is distinct from the manager of the BRC). Only those

personnel that have the appropriate level of access should escort visitors within restricted and high security areas.

6.4. Incident response plan

BRCs should devise and adopt an incident response plan, which sets forth a protocol to be followed by BRC staff for recording, reporting and investigating security breaches. Guided by applicable laws, BRCs should determine how to report investigations of security breaches.

BRCs should ensure that every staff member (including non-technical staff) is fully notified of the incident response plan and trained in the actions they should take in the event of a security breach.

The incident response plan should indicate the reporting requirements in case of a security breach. BRCs should alert the responsible national authorities if a security breach involves biological material with a high or moderate biosecurity risk level, and be prepared to communicate information on associated risks to the local community if so requested by competent national authorities.

For security breaches involving biological material with a high or moderate biosecurity risk level, the incident response plan should identify the internal staff and external national authorities to whom the security breach is to be reported, in what order, and any other actions they need to take. These actions should include immediately instigating appropriate biosafety measures to reduce any health and safety risks to laboratory staff and the local community arising from the breach, and in as far as it is safe to do so, avoid disturbing the scene of the breach and any evidence until authorities arrive.

The incident response plan should identify individuals responsible for retrieving and compiling information that may assist investigating authorities, including where relevant, a list of people who have legitimate access to the material, the biosecurity risk level assigned to the biological material or data compromised (*e.g.* infective dose, pathogenicity, lethality, transmissibility, environmental viability, availability of therapeutic agents) and the inventory of requests received for the material.

6.5. Staff training and developing a biosecurity-conscious culture

BRCs should devise and implement a biosecurity training course to instruct relevant staff (both technical and non-technical staff) in the biosecurity procedures of the facility. The training course should explain to staff the key elements of the Risk Management Practices and ensure that staff are aware of their responsibilities and the procedures that should be followed during the course of their work. The course should give staff specific instruction on what constitutes a breach of security procedures and if appropriate, provide information about disciplinary sanctions that will be applied if a staff member deviates from the BRC's biosecurity policy.

In particular, the course should instruct on the Incident Response Plan, ensuring that all staff are fully aware of the actions they should take if they detect a security breach, or witness activity that they deem suspicious on security grounds.

The biosecurity training course should comprise one element of the general orientation course that new staff typically undergo.

Appropriate risk communication and the creation of a biosecurity-conscious culture in the community are important elements in establishing biosecurity. In addition to undertaking sufficient biosecurity measures, a BRC should conduct its activities in a transparent manner and strive to build trust in its relations with the local community

6.6. Material control and accountability

BRCs should establish a system of material control and accountability, which includes conducting and maintaining inventories of biological materials in their collections and identifies individuals who have access to or custody of biological materials at any point in time.

The system should provide accurate knowledge of what biological materials exist in a BRC, where those materials are, and who has access to them or custody of them at any given time. Material control and accountability applies to all biological materials held by BRCs, including those with only negligible or low biosecurity risk associated with them. Individual vials need not be counted except in the case of high biosecurity risk level materials.

6.7. Supply of material

BRCs may grant requests from facilities that seek to acquire, use and maintain biological material that presents a negligible or low risk, subject to national legislation.

Biological material that presents a moderate or high biosecurity risk should only be transferred to facilities that ensure biosafety and biosecurity measures appropriate to handle such material are in place.

BRCs should document all acquisition requests in particular for high and moderate biosecurity risk level materials, including requests refused and the reason for refusal. BRCs should be able to provide competent national authorities with a record of all acquisition requests for such materials whether the request was accepted or declined, if requested by such national authorities.

In order to bring to light in a timely manner that biological materials have been lost or diverted during transport, BRCs should condition dispatch of biological material with a high or moderate biosecurity risk level upon agreement of the receiving party to provide notice of successful receipt in their as agreed timeframe.

6.8. Transport security

BRCs should institute procedures that secure material during packaging and transport to reduce the risk of theft.

Internal and external transfers of biological material that present a negligible or low biosecurity risk do not require any additional security measures other than those required by national or regional/international regulations.

6.8.1 Internal transport

Biological material that poses a high biosecurity risk should neither be left unattended nor temporarily stored outside the high security area.

BRCs should employ a strict chain of custody approach to the internal transfer of biological material that presents a moderate or high biosecurity risk and movement from one high security

or restricted area, via a restricted or general security area, to another high security or restricted area.

This procedure should aim to be as minimally burdensome as possible while allowing subsequent analysis of the transactions and transfers made within the scope of the preceding paragraph.

6.8.2 External transport

BRCs should follow the WHO Guidelines on International Regulations for the Packaging and Transport of Infectious Substances to ensure safe and secure packaging and transportation of biological material.

Biological material exempt from the WHO guidelines (non-infectious micro-organisms allocated to Risk Group1) may be sent by (air) mail or other means of transport according to the Universal Postal Union (UPU) requirements.

BRCs should follow the International Air Transport Association (IATA) Dangerous Goods Regulations (DGR) and other applicable regulations, including those for road transport, to ensure that all requirements for packaging and shipping dangerous goods on ground and air are met.

BRCs should ensure that staff responsible for the distribution of biological material have the necessary knowledge and training to comply with applicable national and regional/international laws and regulations. Staff responsible for the distribution of dangerous goods (including infectious substances) via air should have the shipper's training certificate as required by IATA.

6.9. Security of information

BRCs should undertake an information risk assessment, to determine what information presents a biosecurity risk and take steps to protect information that could reasonably be used to facilitate the theft of high or moderate biosecurity risk material (*e.g.* access codes).

6.9.1 Information that relates to access to materials

Information that could reasonably be used to facilitate the loss or theft of biological materials with a high or moderate biosecurity risk level should be protected by proportionate measures to ensure the security of this information. The information should be secured against unauthorised access by appropriate physical and/or electronic means (depending on the format in which the information is stored and the resources available to the BRC).

Access to information pertaining to biological materials associated with high or moderate biosecurity risk levels should be granted on a need-to-know basis, and granted only to those individuals with security clearance to access material at the same biosecurity level as the information sought. For example, individuals with clearance to access moderate biosecurity level material should be able to access (if necessary) information up to that security level, but not above.

6.9.2 Information that relates to the collection

BRCs should develop a policy to guide them in deciding what kinds of information relating to the collection should purposefully be withheld from entering the public domain.

The BRC staff should be aware that their repository of knowledge could present a security risk. BRCs may choose to address this issue through encouraging staff to adopt a code of conduct specific to biosecurity.

NOTES

These notes are to be read jointly with their corresponding sections found in the biosecurity best practice guidelines.

Scope

BRCs distinguish between biosecurity and biosafety measures. Biosafety entails the use of containment principles, technologies and practices that are implemented to prevent unintentional exposure to pathogens and toxins, or their accidental release. Biosecurity is intended to deter or detect the loss or theft of dangerous biological materials for illicit or malicious purposes. These biosecurity best practice guidelines focus on preventing unauthorised access to dangerous biological materials in BRCs. They are not intended to address biosecurity in other types of facilities, nor do they address specific measures related to crisis management in the event of a security breach.

Biosecurity risk management practices for BRCs

The biosecurity officer need not be a separate, full-time position; its functions may belong to the responsibilities of the BRC manager or another employee of the BRC.

6.1. Physical security of BRCs

The purpose of physical security measures is to minimize opportunities for unauthorized entry into BRCs, and to prevent the unauthorized removal of materials from their facility. Physical security measures can be manual, such as locks on internal and external doors, freezers and storage cabinets, or electronic, such as electronic access and biometric access controls, or they can be based on manpower (private security guards). Intrusion detection sensors and cameras, although not physical barriers, can provide an instant alert in the case of a security breach. In exceptional circumstances biometric controls may be deemed appropriate.

6.3. Security management of visitors

BRCs possessing high or moderate biosecurity risk material should develop a policy addressing prohibited items for both staff and visitors and inform staff about what particular items are prohibited.

Although escorted visitors generally should not have access to restricted or high security areas, some circumstances (such as essential maintenance work) may require it.

6.4. Incident response plan

The severity of a security breach should be evaluated in accordance with risks that arise as a consequence of it. For example, a missing link in the documented chain of custody should be considered a less severe security breach than unauthorized entry into the facility or misappropriation of biological material.

6.5. Staff training and developing a biosecurity-conscious culture

BRCs should seek to raise awareness of the need to secure biological materials against their unauthorised acquisition and misuse by holding seminars, information campaigns and other

activities as they consider appropriate to the nature of the facility and the tasks performed by their staff. An important component of developing a biosecurity-conscious culture is the development of a code of conduct by staff.

6.7. Supply of material

It is incumbent on the requesting facility, not the BRC, to prove to the BRCs satisfaction that it has put in place biosafety and biosecurity measures appropriate to handle high and moderate biosecurity risk level materials.

6.8.2 External security

The WHO Guidelines may be found at the following web link:
http://whqlibdoc.who.int/hq/1997/WHO_EMC_97.3.pdf.

The International Postal Union requirements may be found at the following web link:
http://ibis.ib.upu.org.

The IATA regulations can be found at the following web link: http://www.IATA.org/cargo/dg.

An example of transport regulations is the European Agreement concerning the International Carriage of Dangerous Goods by Road (ADR regulations). The ADR regulations can be found at the following web link: http://www.unece.org/trans/danger/publi/adr/ADRagree_e.pdf.

6.9.1 Information that relates to access to materials

This includes information pertaining to the facility (physical plans detailing the layout of the facility and the location of the master control of electrical and communication services that are essential for keeping security barriers in place), personal information on employees that could be used for blackmail, sensitive documentation such as a review that points to weaknesses in a facility's security programme, and information that could potentially assist in gaining unauthorised access to biological materials and inventories.

The key question in conducting the information risk assessment is whether possessing the information would permit the holder to severely compromise the health of humans, crops, livestock or infrastructure.

6.9.2 Information that relates to the collection

Information that relates to the collection includes detailed information on organisms, such as that relating to environmental hardiness, aerosolisation, cultivation method, sequence data *etc.* Such information, in particular that relating to organisms that present a high or moderate biosecurity risk, can present a security risk itself.

In deciding what information relates to the collection, BRCs may be guided by the Journal Editors' Statement on Scientific Publication, see: *Security Journal Editors and Authors Group, Proceedings of the National Academy of Sciences* (PNAS), February 18, 2003, Vol. 110, No. 4, pp. 1464.

A source for various laboratory biosecurity codes of conduct can be found at the following web link: http://www.biosecuritycodes.org/.

BEST PRACTICE GUIDELINES FOR THE MICRO-ORGANISM DOMAIN

1. Introduction

These domain specific best practice guidelines provide the basis for best practices in the management of Biological Resource Centres (BRCs) that hold and supply micro-organisms.

All BRCs must comply with applicable national and international laws and regulations. These domain specific best practice guidelines provide best practice for managing BRCs and describe the procedures for acquisition, propagation, maintenance and provision of micro-organisms. Best practice requires a BRC to provide a documented description of the nature of the micro-organism domain biological resources being held and in particular to define the level of hazard and containment in place.

These domain specific best practice guidelines assist the BRC to put into practice procedures that comply with relevant national law, regulations and policies. Further practical details on the implementation of these procedures may be found in the Common Access to Biological Resources and Information (CABRI) guidelines: (http://www.cabri.org), World Federation for Culture Collections (WFCC) recommendations: http://www.wfcc.info/ or United Kingdom National Culture Collection (UKNCC): www.ukncc.co.uk.

2. Scope

The purpose of this document is to help ensure that micro-organisms held and supplied by BRCs are of the highest standard and authentic. The methods used should be such that the key features of micro-organisms maintained are retained and should ensure their consistency amongst BRCs supplying them. This will help to provide a reliable basis for research and development in different laboratories and will contribute towards protection of the health of laboratory personnel, the public and the environment.

3. Definitions

The definitions in the document *General Best Practice Guidelines for all BRCs* apply with the following additions:

3.1. Micro-organisms

"Micro-organisms" comprise all prokaryotes (archaea and bacteria), some eukaryotic organisms (fungi, yeasts, algae, protozoa), non-cellular entities (*e.g*. viruses), their replicable parts and other derived materials *e.g*. genomes, plasmids, cDNA.

3.2. Biological material

The term "biological material" used throughout this text refers to micro-organisms and their derived materials as defined in 3.1 above.

4. Specific BRC Best practice guidelines

4.1. Staff - qualifications and training

Staff should have relevant qualifications, training and competence to carry out their duties.

4.2. Health and safety

All staff should follow the procedures laid down under the appropriate level of containment for the micro-organisms being handled, as defined by the World Health Organisation (WHO, 2004) and as interpreted by national law, regulations and policies, to avoid contaminating samples, risk of infection and environmental dispersion.

5. Premises

It is the responsibility of the entity which comprises the BRC, or, within which the BRC is located, to provide an environment that is conducive to handling micro-organisms, for example, free from contamination.

5.1. Construction and operation

Construction should respect the containment level appropriate for the risk group of the micro-organisms worked with and should meet appropriate national law, regulations and policies. If major building, renovation or repair work, or other work that is likely to compromise containment or clean conditions, is necessary in Biological Resource Centres, normal activities should be suspended until the building renovation or repair work is completed.

5.2. Maintenance and inspection

Cleaning of laboratory benching and equipment should be performed by authorised and trained staff using appropriate personal protection equipment and following documented procedures. A contamination monitoring programme should be in place to include environmental monitoring of laboratory air and surfaces. If a major contamination problem arises in the BRC, the BRC manager should be responsible for implementing a cleaning programme and an investigation of the source of contamination. Details of decontamination procedures should be located in a Procedures Manual or relevant Standard Operating Procedures (SOPs). Quality audit and quality review should be carried out.

6. Equipment use, calibration, testing and maintenance records

As set out in *General Best Practice Guidelines for all BRCs*.

Appropriate maintenance and calibration procedures for common items of equipment used in microbial domain BRCs are summarised in Table 1 of the Appendix.

7. Informatics

BRCs should follow informatics best practice guidelines as set out in *General Best Practice Guidelines for all BRCs*.

There should be a minimum amount of information available for each accession in the collection (Minimum Data Set (MDS). Additional data may be included in the Recommended Data Set (RDS) and Full Data Set (FDS). The MDS and RDS are listed in Table 2 of the Appendix.[10] The MDS comprises essential information to identify a unique item in the BRC. The RDS includes useful information for an improved description of the material. The FDS provides all remaining

10. The MDS, RDS and FDS are drawn from CABRI Guidelines http://www.cabri.org/guidelines.html.

information that is available at the BRC for any given biological materials. The MDS should always be recorded and made available whereas the RDS is recommended, and the FDS is additional optional information.

8. Preparation of media and reagents

Accurate preparation and storage conditions of culture media, one of the fundamental steps in the growth and maintenance of biological materials, should be given special attention. The BRC should have defined standards for all preparations; media formulae should be documented and procedures put in place to make changes to procedures and for their approval and adoption. Media batches should be clearly labelled and expiry dates (date after which media and reagents are not to be used) defined and clearly indicated.

9. Accession of deposits to the BRC

9.1. Receipt and handling of biological materials

The BRC should document and implement safe procedures for receipt and storage appropriate to the type of biological materials handled. All incoming parcels that contain known or unknown micro-organisms should be opened in a suitable containment laboratory or appropriate microbiological safety cabinet with local facilities for the safe handling and disposal of biological materials.

The depositor should provide assurance that biological materials were obtained legitimately. Conditions of deposit should be determined and agreed *e.g.* laid down in a material transfer agreement (MTA), for example to protect assigned intellectual property rights (IPRs). Where deposits are outside the expertise of the BRC, alternative suitable BRCs should be recommended.

Quality control procedures should be carried out upon receipt of biological material to confirm its purity, identity and viability. The recommended procedures that should be carried out are in Table 3 of the Appendix.

Before accepting a deposit, the BRC should check against risk group lists and other lists to make sure that the biological material does not exceed the laboratory's biological safety containment level.

10. Preservation

10.1 Long-term preservation

The commonly used approach for sustainable preservation of microbial cultures is long-term preservation employing liquid nitrogen, deep freezing, freeze-drying or L-drying methods. These methods allow high quality long-term storage, recovery and use of the micro-organism. For each micro-organism culture, an appropriate preservation method(s) should be chosen by the BRC based on its own experience or on the recommendations of the depositor (see section 10.2). The methods used should be equivalent to those cited above and should ensure:

- High viability/recovery of the preserved culture.
- No contaminant in the preserved culture (this does not include any recognised co-culture *e.g.* symbiotic micro-organisms), which are not regarded as contaminants so

long as the constituents are correctly specified and checked by microbiological and molecular analysis, as applicable).

- Authenticity of the preserved culture and genome integrity (molecular, phenotypic analysis), where applicable.

The recommended methods for the storage and preservation of biological materials and the form in which it is distributed are set out in Table 4 of the Appendix.

10.2. Validation of methods and procedures

Validation of the methods and procedures used for preservation should be carried out to ensure their reproducibility and reliability, and general compliance during the quality control of biological material. Performance of the method(s) should correspond to the criteria listed in Section 10.1.

In addition to the requirements laid out in the *General Best Practice Guidelines for all BRCs,* the validation of quality check, characterisation and preservation methods should be carried out by using at least one of the following approaches:

- Performing blind tests.
- Comparing the results of the same method performed at different times (reproducibility).
- Comparing results obtained with different methods (reliability).
- Comparing the results obtained for the same method performed by different persons.

The results of quality checks and the procedure used should be recorded.

11. Supply of material

The means to ensure secure supply of biological material by BRCs are set out in *Best Practice Guidelines on Biosecurity for BRCs*. The best practices set out in these guidelines supplement the best practices detailed below.

11.1. Order placement

To the extent that it can be determined, BRCs should supply micro-organisms only to laboratories and only to those individuals who are trained in microbiology and have access to properly equipped laboratories, unless otherwise justified and documented. First orders from new clients should be received on an order form with the client's official letterhead and signed by an authorised person. The BRC should accept fax and mail orders with an official user order number unless signature and/or permits are required for release of particular biological materials. E-mail and telephone orders could be accepted from known or registered users where signatures of authority are not required.

11.2. User validation

To ensure that only authorised users may access biological material that is pathogenic or toxic to humans, animals and plants, the BRC should implement any national and international requirements and, as applicable, the following measures for the respective hazardous material:

- Comply with the measures set out in *Best Practice Guidelines on Biosecurity for BRCs*.
- Check that the name and signature of the head of department/division match against those registered in the BRC's list of authorised institutions.
- Check that the name and signature of the user match against those registered in the BRC's list of authorised users.
- Have written and signed documentation proving that the user has the appropriate containment facilities and the authorisation to import and handle such biological material.

An order should only be processed when the required accompanying documentation is completed, signed and returned.

11.3. Availability of the biological material ordered

Freeze-dried or cryo-preserved (when supplied frozen) material should be dispatched as soon as possible once necessary licenses and/or documentation are provided. Dispatch for such materials should be according to the laid down procedures and conditions. Where materials cannot be delivered within three working days (*e.g.* actively growing cultures), then the client should be informed of the delay within three working days.

11.4. Packaging and Transport

The packaging of biological material and its transport by postal and other transport services is controlled by international and regional agreements and national laws.

To ensure safe and secure packaging and transportation of biological material, BRC should follow the WHO Guidelines on International Regulations for the Packaging and Transport of Infectious Substances.[11] These best practice guidelines provide practical guidance to facilitate compliance with current international regulations for the transport of infectious substances by all modes of transport, both nationally and internationally.

Those materials exempt from the WHO guidelines (non-infectious micro-organisms allocated to Risk Group 1 may be sent by (air) mail or other means of transport according to the Universal Postal Union (UPU) requirements.[12]

The International Air Transport Association (IATA) Dangerous Goods Regulations (DGR) are legally binding for shippers and carriers of dangerous goods (including infectious substances) to be transported by air. For transportation via road, rail and waterways, regional and/or national regulations exist. BRCs should follow the IATA DGR and other respective regulations, to ensure

11. www.unece.org/trans/danger/publi/unrec/rev13/

12. http://ibis.ib.upu.org

that all applicable requirements for packaging and shipping dangerous goods on ground and air are met.[13]

BRCs should ensure that staff responsible for the distribution of biological material have the necessary knowledge and training.

Staff responsible for the distribution of dangerous goods (including infectious substances) via air should have the shipper's training certificate as required by IATA.

11.5. Traceability of hazardous biological materials

The BRC should maintain individual records of all requests for hazardous biological materials – including those requests refused for any reason – showing the biological material, method and date of shipment, and name and address of the person to whom sent.

12. Micro-organism Biological Resource Centres' compliance with national and international law

Micro-organisms are isolated, grown, characterised, preserved for the long-term, stored and transported between laboratories. They are shipped by various means, by postal mail or by courier service, from one laboratory to another within countries, and often across borders or continents. They are sent for identification, reference, research or for production purposes from colleague to colleague, from and to culture collections. All these actions should be carried out safely and in compliance with the various legislation and regulations that control these matters. The BRC should ensure that any changes to applicable legislation and regulations are implemented in their procedures.

The importance of a laboratory's health and safety procedures extend beyond the laboratory to all those who come in contact with substances and products from that laboratory. A micro-organism in transit might put carriers, postal staff, freight operators and recipients at risk, some organisms being relatively hazard free whilst others can be quite dangerous. Safety and shipping regulations should be followed to ensure safe transit. The BRC should adhere to regulations relevant to the distribution of micro-organisms.

A Biological Resource Centre (BRC) should, for example**,** comply with:

- Applicable health and safety requirements.
- Classification of micro-organisms on the basis of risk.
- Applicable quarantine regulations.
- Intellectual property rights (IPR).
- Requirement that safety information is provided to the recipient of micro-organisms.
- Applicable regulations governing shipping of cultures.
- Control of distribution of biological material.

13. http://www.IATA.org/cargo/dg

- Provision of appropriate safety information to the recipient of micro-organisms.

In the process of isolation, handling, storage and distribution of micro-organisms, there are many stages where compliance with the law, regulations or voluntary international conventions is required. Table 5 of the Appendix lists some examples of these.

Whether it is compliance with the law, or duties of a caring employer, essential components for a safe workplace are:

- Adequate assessment of risks.
- Provision of adequate control measures.
- Provision of health and safety information.
- Provision of appropriate training.
- Establishment of record systems to allow safety audits to be carried out.
- Implementation of good working procedures.

Best practice requires BRCs to have and implement a sound health and safety plan.

12.1. Classification of micro-organisms according to risk groups

Various classification systems exist and are implemented nationally. The key references are the definitions for classification made by the World Health Organisation (WHO). The definition and minimum handling procedures of pathogenic organisms are set by appropriate authorities in each country.

The WHO classifies micro-organisms into four groups according to the risk they impose to humans:

Risk group 1: (no or low individual and community risk). A micro-organism that is unlikely to cause human or animal disease.

Risk group 2: (moderate individual risk, low community risk). A pathogen that can cause human or animal disease but is unlikely to be a serious hazard to laboratory workers, the community, livestock or the environment. Laboratory exposures may cause serious infection, but effective treatment and preventive measures are available and the risk of spread of infection is limited.

Risk group 3: (high individual risk, low community risk). A pathogen that usually causes serious human or animal disease but does not ordinary spread from one infected individual to another. Effective treatment and preventive measures are available.

Risk group 4: (high individual and community risk). A pathogen that usually causes serious human or animal disease and that can be readily transmitted from one individual to another, directly or indirectly. Effective treatment and preventive measures are not usually available.

A BRC should ensure that all biological materials are assigned to appropriate risk groups; this includes a positive assignment to Risk Group 1 unless otherwise considered hazardous. Risk group information should be recorded and made available to recipients of biological material.

12.2. Quarantine regulations

Clients, who wish to obtain cultures of plant pathogens underlying quarantine regulations should first obtain a permit to import, handle and store from the appropriate authority. Under the terms of such a licence the shipper is required to see a copy of a permit before such strains can be supplied.

Plant pathogens handled by BRCs that are subject to quarantine regulations should be registered by an appropriate governmental office. Import and transfer of such pathogens within the country should be carried out according to relevant law.

12.3. Intellectual Property Rights (IPRs)

On deposit of a micro-organism, BRCs should record terms and conditions for its further distribution.

Transparency, retaining the link between the source and all recipients of biological materials, is the preferred practice. Where appropriate, material transfer agreements should be put in place.

12.4. Safety information provided to the recipient of micro-organisms

Safety information should be dispatched with a micro-organism indicating which risk group it belongs to and what containment and disposal procedures are necessary. For a micro-organism, a safety data sheet should include:

- The risk group of the organism being dispatched.
- A definition of the risks and assessment of the risks involved in handling the organism.
- Requirements for the safe handling and disposal of the micro-organism.
- Containment level.
- Opening procedure for cultures and ampoules.
- Appropriate transportation of the micro-organism.
- Procedures in case of spillage.

12.5. Control of Distribution of Hazardous Micro-organisms

BRCs should follow the *Best Practice Guidelines on Biosecurity for BRCs*.

There is considerable concern over the transfer of certain infectious agents capable of causing substantial harm to human health. There is potential for such organisms to be passed to parties not equipped to handle them or to people who may make illegitimate use of them. To reduce the risk a BRC should have procedures in place which meet national requirements to check the validity of customers that wish to receive hazardous organisms.

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EC Council Directive 95/44/EC on establishing the conditions under which certain harmful organisms, plants, plant products and other objects listed in Annexes I to V to Council Directive 77/93/EEC may be introduced into or moved within the Community or certain protected zones thereof, for trial or scientific purposes and for work on varietal selections.

EC Council Directives 90/219/EEC and 98/81/EC on contained use of genetically modified organisms.

EC regulation 1946/2003 on the transboundary movement of genetically modified organisms (pertains to Cartagena Protocol on Biosafety).

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ISO 7218:2000, Microbiology of food and animal feeding stuffs. General rules for microbiological examinations.

ISO 9001:2000, Quality Management Systems – Requirements.

ISO 17025:2005, General requirements for the competence of testing and calibration laboratories.

Kirsop, B.E. & Doyle, A. (eds) (1991). Maintenance of Microorganisms and Cultured Cells: A Manual of Laboratory Methods, London: Academic Press.

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Smith, D, Rohde, C (2002). The implication of the biological and toxin weapons convention and other related initiatives for WFCC members. WFCC Newsletter 34: 4-11.

Technical Instructions for the Safe Transport of Dangerous Goods by Air. Doc 9284-AN/905. Council of ICAO, International Civil Aviation Organisation.

United Kingdom National Culture Collection (1998) Quality manual. UKNCC Secretariat CABI Bioscience UK Centre, Egham, UK.

Universal Postal Convention, Compendium of Information, Bern (International Bureau), Universal Postal Union, Beijing, 2000.

World Federation for Culture Collections (1999). Guidelines for the establishment and operation of collections of cultures of micro-organisms. UK: WFCC Secretariat. (2nd ed.).

WHO World Health Organization, Geneva, Nonserial Publication, ISBN: 92 4 154650 6. Laboratory Biosafety Manual, Third Edition, English, 2004.

WEBSITES OF INTEREST FOR INFORMATION

This list will require periodic update; BRCs should review information available to assist them in compliance with legislation and best practice in the operation of the BRCs.

Transport and shipping

International Laboratory Accreditation Cooperation (ILAC)	http://www.ilac.org/
Micro-Organisms Sustainable use and Access regulation International Code of Conduct	www.belspo.be/bccm/mosaicc
CABRI Guidelines	http://www.cabri.org/gidelines.html
Canadian Transport	www.rural-gc.agr.ca/e4.1_canutec.html
European Commission DGVII – Transport	http://europa.en.int/en/comm/dg07/index.htm
Harmonisation of UN documents etc.	www.hazmat.dot.gov/rules
International Air Transport Association	www.IATA.org/cargo/dg www.IATA.org/cargo/dg/links.htm
International Civil Aviation Authority	http://hazmat.dot.gov/icao.htm www.volpe.dot.gov/ohm/icao.htm www.cam.org/~icao/menu3.html
Maritime rules	www.eat.co.uk/ncec/complian/bibliog/bysea.html www.mdnautical.com/imo/cargoes.htm www.imo.org/pubs/pubcats.htm www.info.gov.hk/mardep/notices/mdn98149.htm www.hazmathelp.com/imdg.htm
The European Agreements Concerning the International Carriage of Dangerous Goods by Rail (RID) and by Road (ADR)	http://hazmat.dot.gov/RIDADR.htm www.dsidat.com/products/undisk7.htm www.volpe.dot.gov/ohm/ridadr.htm
Transport – general	www.tci-transport.fr
German magazine	www.hazmathelp.com/dotlink.htm www.cefic.org www.storck-verlag.com/english/gela_e.htm
United Nations meetings agenda and minutes	www.unece.org/unece/trans/danger/meetdoc.htm
UN Model Regulations	www.unece.org/unece/trans/main/dgdemo/intro.htm
UN Committee of Experts	www.tc.gc.ca/tdgoods/consult/unlinks_e.htm
Universal Postal Union	http://ibis.ib.upu.org http://unicc/unece/tra www.de/facil/upustr.htm

WHO Guidance on Regulations for the Transport on Infectious Substances	http://www.who.int/csr/resources/publications/biosafety/WHO_CDS_CSR_LYO_2005_22/en/

Biosafety

Organisation for Economic Co-operation and Development (OECD)	http://www.oecd.org/dataoecd/4/4/34932656.pdf
United Nations Industrial Development Organisation (UNIDO) Bio-safety Information Network and Advisory Service (BINAS)	www.who.org/emc/biosafe/index.htm
International Centre for Genetic Engineering and Biotechnology (ICGEB)	www.aphisweb.aphis.usda.gov.biotech
US Animal and Plant Health Inspection Service (APHIS)	www.nal.usda.gov/bic/
US Food and Drug Administration (FDA)	http://www.fda.gov/
World Health Organization (WHO) Biosafety Programme	http://www.who.int/csr/labepidemiology/projects/biosafetymain/en/index.html
U.S. Departments of Health and Human Services (HHS) and Agriculture (USDA) rules implementing USA PATRIOT Act and Public Health Security and Bioterrorism Preparedness and Response Act of 2002	http://www.cdc.gov/od/sap/final_rule.htm
Centre for Food Safety and Applied Nutrition (CFSAN)	http://vm.cfsan.fda.gov/list.html
Belgian Bio-safety Server	www.biosafety.be
The Dutch Genetically Modified Organism Bureau	www.rivm.nl/csr/bggo.html
Biotechnology Information Centre (BIC) of the US Department of Agriculture (USDA)	www.nal.usda.gov/bic/
UK Advisory Committee on Releases into the Environment (ACRE)	www.environment.detr.gov.uk/acre/index.htm
National Chemical Emergency Response UK	www.eat.co.uk/ncec/complian/bibliog/bibliog.htm
American Biological Safety Association (ABSA)	http://www.absa.org
European Biosafety Association (EBSA)	http://www.ebsaweb.eu
International Biosafety Working Group (IBWG)	http://www.internationalbiosafety.org/english/index.asp

Advisory Committee on Dangerous Pathogens http://www.doh.gov.uk/bioinfo.htm

Biodiversity

Convention on Biological Diversity: http://www.unep.org/biodiv.html

International Organisations

World Federation for Culture Collections: http://www.wfcc.info/

World Data Centre for Micro-organisms: http://wdcm.nig.ac.jp/

Common Access to Biological Resources and Information: http://www.cabri.org

European Biological Resource Centres Network: http://www.ebrcn.org

ASM – Asian Consortium for the Conservation and Sustainable Use of Micro-organisms http://www.abrcn;net

ECCO, European Culture Collection Organisation: http://www.eccosite.org

Food and Agriculture Organization (FAO): http://www.fao.org/

World Animal Health Organization (OIE): http://www.oie.int/eng/en_index.htm

International Plant Protection Convention (IPPC): https://www.ippc.int/IPP/En/default.jsp

International Police Organization (INTERPOL): http://www.interpol.int/

The Australia Group: http://www.australiagroup.net/

Biological Weapons Convention (BWC): http://disarmament.un.org/wmd/bwc./

MIRCEN Scholarships:http://portal.unesco.org/sc_nat/

UNESCO People, Biodiversity and Ecology http://www.unesco.org/mab/index.shtml

WIPO - World Intellectual Property Organization : http://www.wipo.int

ISO - International Organization for Standardization: http://www.iso.ch/iso/en

Patents

Budapest Treaty on the International recognition of the Deposit of Micro-organisms: http://www.wipo.int/treaties/en/registration/budapest/

Taxonomy and Nomenclature ICSP

International Committee on Systematics of Prokaryotes (ICSP): http://www.the-icsp.org/

Bacterial Nomenclature up-to-date: http://www.dsmz.de/bactnom/bactname.htm

Species 2000 Indexing Project: http://www.sp2000.org

List of bacterial names with standing in nomenclature: http://www.bacterio.cict.fr/

Viruses' names: http://www.ncbi.nlm.nih.gov/ICTVdb/;
http://www.micro.msb.le.ac.uk/3035/virusgroups.html

Fungal names: http://www.ukncc.co.uk

Bacterial Code of Nomenclature: http://www.the-icsp.org/Code history.htm

Index Fungorum: http://www.indexfungorum.org

APPENDIX

Table 1. Maintenance and Calibration Requirements for Equipment Commonly Used in BRCs

Item	Maintenance required	Verification of function
Autoclaves	Cleaning, pressure vessel, system of surveillance, maintenance contract as required; run with indicators	As recommended by manufacturer
Incubators	Cleaning, system of surveillance, maintenance contract as required	Manufacturers' standard on service
Liquid nitrogen storage vessels	Cleaning, leakage, pressure	Once yearly Manufacturers' Test
Centrifuges	Cleaning, system of surveillance, maintenance contract as required	Regular cleaning Manufacturers' service
Cryo-storage tanks	Removal of condensation and ice	
LN_2 store oxygen level alarm	System of surveillance, maintenance contract as required	Manufacturers' standard on service
LN_2 level alarms	Look for malfunction	None
Programmed Cooler	System of surveillance, maintenance contract as required	None
Cryomicroscope	Clean after use, Temperature calibration	Calibration equipment provided for test at each time of use
Spin and shelf freeze-drier	System of surveillance, maintenance contract as required	Calibration of the vacuum gauge
Microscopes	Clean after use, System of surveillance, maintenance contract as required	
Laminar Flow Cabinet	Clean after use, airflow	Annual functionality test
Class II Microbiological Safety Cabinet	Clean after use System of surveillance, maintenance contract as required	Manufacturers' standard on service
-20 °C Freezer	Temperature check	None
-80°C Freezer	Temperature check and registration System of surveillance, maintenance contract as required Security advices	
Media Preparation equipment	Clean after use	
Balance	System of surveillance, maintenance contract as required Clean after use	Manufacturers' standard on service
pH Meter	Clean after use	Test against Manufacturers' standard

LN_2 = Liquid Nitrogen

Table 2. Minimum Data Sets (MDS) and Recommended Data Sets (RDS) for Microbial Accessions to BRCs

Filamentous fungi	**Filamentous fungi**
Minimum Data Set (MDS)	**Recommended Data Set (RDS)**
Accession number	Misapplied names
Other collection numbers	Isolated from
Name	Mutant
Organism type	Literature
Restrictions	Sexual state
Status	Race
History of deposit	
Conditions for growth	
Form of supply	
Geographic origin	
Yeasts	**Yeasts**
Minimum Data Set (MDS)	**Recommended Data Set (RDS)**
Accession number	Isolated from
Other collection numbers	Mutant
Name	Sexual state
Organism type	Literature
Restrictions on distribution	Misapplied names
Status	Race
History of deposit	
Geographic origin	
Conditions for growth	
Form of supply	
Microalgae	**Microalgae**
Minimum Data Set (MDS)	**Recommended Data Set (RDS)**
Accession number	Literature
Other collection number	Conditions for storage
Name and taxonomy	Isolate history
History of deposit	
Isolate history	
Form of supply	
Geographic origin	
Conditions for growth	
Bacteria	**Bacteria**
Minimum Data Set (MDS)	**Recommended Data Set (RDS)**
Accession number	Serovar
Other collection numbers	Other names
Name	Isolated from
Infrasubspecific names	Mutant
Organism type	Genotype
Restrictions on distribution	Literature
Status	
History of deposit	
Geographic origin	
Conditions for growth	
Form of supply	

Table 2. Minimum (MDS) Data Sets and Recommended (RDS) for Microbial Accessions to BRCs (*cont.*)

Cyanobacteria	**Cyanobacteria**
Minimum Data Set (MDS)	**Recommended Data Set (RDS)**
Accession number	Other names
Other collection numbers	Isolated from
Name and taxonomy	Mutant
Infrasubspecific names	Genotype
Organism type	Literature
Restrictions on distribution	
Status	
History of deposit	
Conditions for growth	
Form of supply	
Geographic origin	
Archaea	**Archaea**
Minimum Data Set (MDS)	**Recommended Data Set (RDS)**
Accession number	Other names
Other collection numbers	Isolated from
Name	Mutant
Infrasubspecific names	Genotype
Organism type	Literature
Restrictions on distribution	
Status	
History of deposit	
Geographic origin	
Conditions for growth	
Form of supply	
Plasmids	**Plasmids**
Minimum Data Set (MDS)	**Full Data Set (FDS); RDS is not applicable**
Collection Accession number	Constructed from
Name	Incompatibility group
Other culture collection numbers	Transfer ability
Type	Helper
Class	Copy number
Literature	Molecular weight
History of deposit	Cloned gene
Restricted distribution	Transposable element
Host for distribution	Promoter
Medium	Ribosome binding site
Selectable phenotype	Start codon
Replicon	Terminator
Host range	Further information (Remarks on propagation and/or on properties and/or on history, other name(s), etc)
	Restriction sites
	Sequence detail
	Price code
	Properties and application

Table 2. Minimum (MDS) Data Sets and Recommended (RDS) for Microbial Accessions to BRCs (*cont.*)

Protozoa	**Protozoa**
Minimum Data Set (MDS)	**Recommended Data Set (RDS)**
Accession number	Biochemical or molecular characteristics
Other collection numbers	Other name
Name	Substrate or host
Organism type	Year of isolation
Stage	Literature
History of deposit	
Status	
Restriction on distribution	
Conditions for growth	
Form of supply	
Geographic origin	
Phages	**Phages**
Minimum Data Set (MDS)	**Recommended Data Set (RDS)**
Accession number	Cell surface receptor
Element name	
Element type	
Other culture collection numbers	
Restricted distribution	
Literature	
History of deposit	
Host for propagation	
Host used for propagation	
Lysogenicity	
Virus used for	
Viruses	**Viruses FDS = MDS**
Minimum Data Set (MDS) = Full Data Set (FDS)	
Accession number	
Virus name	
Virus name abbreviation	
Former name	
Genus	
Pathotype, serotype, strain	
Original host	
Geographic origin	
Isolate history	
Reference isolate	
Quarantine regulations	
Remarks	
cDNA and gDNA Libraries	**cDNA and gDNA Libraries, MDS = RDS**
Minimum Data Set (MDS)	
Library Name	
Organism	
Type (cDNA or gDNA)	
Vector	
Insert Size	
Library Coverage	

Table 3. Quality control procedures recommended for micro-organisms upon receipt

Micro-organism	Viability	Purity	Identity	Stability
Plasmids	Confirm presence by growing the host/plasmid combination on appropriate selective medium.	Check the texture, the size and the opacity of the colonies grown on selective medium. Check also for homogeneity of the colonies and for absence of contaminants.	Check plasmid length by determination of the molecular weight of the covalently closed circle (ccc) DNA or by analysis of the restriction site pattern.	Confirm presence by growing the host/plasmid combination on appropriate selective medium. Confirm presence by PCR for cryptic plasmid.
Yeasts and Filamentous fungi	Check growth on appropriate medium.	Check for absence of contaminants using macro- and microscopic observations on the culture grown on appropriate medium.	Identify to species level using morphological (macroscopic and microscopic) and physiological features, where appropriate use biochemical features and molecular tools dependant on the taxa.	Check viability and purity. Confirm identity.
Bacteria	Check growth on appropriate medium.	Check for absence of contaminants using macro- and microscopic observations on the culture grown on appropriate medium.	Identify to species level using morphological (macroscopic and microscopic), and physiological tools, where appropriate, use molecular tools.	Check viability and purity. Confirm identity.
Cyanobacteria	Check growth on appropriate medium.	Check for absence of contaminants using macro- and microscopic observations on the culture grown on appropriate medium or specific contaminant medium.	Identify to genus level using morphological (macroscopic and microscopic), and physiological tools, where appropriate, use molecular tools.	Check viability and purity. Confirm identity.

Table 3. Quality control procedures recommended for micro-organisms upon receipt (*cont.*)

Archaea	Check growth on appropriate medium.	Check for absence of contaminants using macro- and microscopic observations on the culture grown on appropriate medium.	Identify to species level using morphological (macroscopic and microscopic), and physiological tools, where appropriate, use molecular tools.	Check viability and purity. Confirm identity.
Viruses	Test infectivity to indicator hosts and propagation hosts.	Use electron microscopic observations.	Combine host reaction, electron microscopic observations and reaction with specific antisera. Where appropriate, use molecular tools.	
Phages	Test infectivity to indicator propagation host.	Test plaque morphology, use electron microscopic observations, test host spectrum.	Test plaque morphology, use electron microscopic observations, test host spectrum.	Test phage titre (pfu/mL)
Microalgae	Check growth on appropriate medium.	Check for absence of contaminants using macro- and microscopic observations on the culture grown on appropriate medium.	Identify to species level using morphological (macro- and microscopic) features and where appropriate use physiological and molecular tools dependant on the taxa.	Check viability and purity. Confirm identity.
Protozoa	Check growth on appropriate medium.	Check for absence of contaminants using macro- and microscopic observations on the culture grown on appropriate medium or specific contaminant medium.	Identify up to species level using morphological (macroscopic and microscopic), and/or where appropriate use biochemical features and molecular tools dependant on the taxa.	Check viability and purity. Confirm identity.
DNA libraries			For DNA libraries, analysis of the restriction site patterns. For individual clones of ordered DNA libraries, identity done by sequencing.	

Table 4. Recommended preservation methods and distribution forms

	Preservation	Distribution forms	Useful information
Plasmids	Two of the following methods : Cryopreservation of the H/P below -70°C. Cryopreservation of the H/P in LN_2. Freeze-drying of the H/P. Preservation of the plasmid DNA (preferably precipitated under ethanol) can also be applied as a preservation method.	Actively growing H/P on agar slant Actively growing H/P in liquid medium Cryopreserved H/P in dry ice Freeze-dried H/P Pure DNA	Plasmids containing genes that may tend to destabilise the physical and/or functional integrity (either by insertion, deletion or point mutation) should preferably be deposited, maintained, tested and delivered as pure DNA.
Yeasts and Filamentous fungi	Two of the following methods : Cryopreservation below –140°C is preferred Cryopreservation below –80°C is accepted Freeze-drying or L-drying of the strain Sporulating-strains should be maintained by at least two of the four different preservation methods listed, one of which should be cryopreservation or freeze drying Non-sporulating strains will be maintained under oil or water or freeze drying and cryopreservation.	Actively growing strain on agar slant Freeze-dried or L-dried material in vials sealed under vacuum or inert gas Cryopreserved material in dry ice. Suspensions in liquid Liquid suspension deposited on filter paper	-
Bacteria	Two of the following methods : <u>Cryopreservation</u> below -140°C is preferred in a freezer below -80°C is accepted <u>Drying:</u> L-drying Shelf-freeze-drying Vacuum drying Spin-freeze drying	Actively growing strain on agar slant Freeze-dried or L-dried material in sealed vials Cryopreserved material in dry ice	-

Table 4. Recommended preservation methods and distribution forms (*cont.*)

Cyanobacteria	Two of the following methods : L-drying Cryopreservation in or above liquid nitrogen, in ultra low temperature (below -140°C) or on agar slant Freeze drying Serial transfer (if long term preservation is not possible)	Actively growing strain on agar slant Actively growing strain on liquid medium Cryo-preserved material in dried ice Freeze-dried material in sealed vials	-
Archaea	Two of the following methods : Cryopreservation below -140°C is preferred below -80°C is accepted L-drying Freeze-drying	Actively growing strain Freeze-dried or L-dried material in sealed vials Cryopreserved material in dry ice	-
Viruses	Two of the following methods : Virus maintenance in situ LN2 Freeze-drying	Freeze-dried material in sealed vials Cryopreserved material in dry ice	-
Phages	Two of the following methods: LN2 L-drying on filter paper in glass ampoule Storage of aliquots at -4°C	LN2-aliquots at ambient temperature or in dry ice Freeze-dried material is sealed ampoule Liquid aliquot (refrigerator)	-
Microalgae	Two of the following methods : Sterile liquid medium Sterile semi-solid medium (agar, alginate beads) Cryopreservation below –140°C	Actively growing in liquid/semi-solid medium Cryopreserved material in dry ice	-
Protozoa	Cryopreservation in or above liquid nitrogen below –140°C	Actively growing strain on liquid medium, or in animal biological liquid. Cryopreserved material in dry ice	-
DNA libraries	Two of the following methods: Cryopreservation of the H/P below -70°C Cryopreservation of the H/P in LN2 Freeze-drying or L-drying Preservation of the DNA precipitated under ethanol	Pure DNA Actively growing H/P Cryopreserved H/P in dry ice Freeze-dried H/P	-

H/P = host/plasmid combination; LN_2 = liquid nitrogen

Table 5. Summary of key elements of national and international regulatory controls related to micro-organism domain BRCs

Action	Requirement	Law, Regulation, Convention	Further information
Collecting in the field	Prior Informed consent from a recognised authority	Convention on Biological Diversity	http://www.biodiv.org
	Mutually agreed terms on use	Convention on Biological Diversity	http://www.biodiv.org
	Consent from the land owner	Property law	
Import	Non-indigenous plant pathogens require licenses from country authority	Quarantine regulations	
	Human, animal and plant pathogens can often only be imported to specified laboratories	Health and Safety	
Handling: Manipulation; Growth	Containment dependent on hazard	Control of Biological Agents - Health and Safety EC Directive 2000/54/EEC on Biological Agents	http://www.brad.ac.uk/acad/sbtwc/btwc/nat_imp/leg_reg/uk/ec_com_2000_54.pdf#search='EC%20Directive%202000/54/EEC%20on%20Biological%20Agents
Genetic manipulation	Containment of manipulated organisms	Council Directive 98/81/EC from October 26th amending Directive 90/219/EEC on the contained use of genetically modified micro-organisms Directive 2001/18/EC of the European Parliament and of the Council on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC Cartagena Protocol on Biosafety	http://www.biodiv.org/biosafety/protocol.asp http://www.biosafety.be/GB/Dir.Eur.GB/Cont.Use/90.219/TC.html http://www.biosafety.be/GB/Dir.Eur.GB/Cont.Use/98_81/98_81_TC.html
Deposit as part of a patent process	Long-term storage and compliance with the Budapest Treaty	Budapest Treaty on the International Recognition of the Deposit of Micro-organisms for the Purposes of Patent Procedures	http://www.wipo.int/treaties/en/registration/budapest/

Table 5. Summary of key elements of national and international regulatory controls posting to micro-organism domain BRCs(*cont.*)

Storage	Appropriate containment	Health and Safety Licence to hold pathogens Security	
Export to another country	Some plant and animal pathogens require export licences	Quarantine regulations	
	Dangerous organisms with potential for dual use	Export Licences for dangerous organisms, Biological and Toxin Weapons Convention (BTWC)	http://binas.unido.org/binas/regs.php http://www.opbw.org/convention/documents/btwctext.pdf http://www.dfat.gov.au/isecurity/pd/pd_4_96/pd9.html
Distribution	Packaging and transport considerations	IATA Dangerous Goods Regulations (DGR), Universal Postal Union (UPU) United Nations Committee of Experts on the Transport of dangerous goods	http://www.iata.org/cargo/dg/dgr.htm http://www.upu.int/ http://www.unece.org/trans/danger/danger.htm
	Sovereign rights over the strains	Convention on Biological Diversity	http://www.biodiv.org
	Access and benefit sharing	Bonn Guidelines	http://www.biodiv.org
	Intellectual Property Right	Patent Cooperation Treaty (PCT) The Budapest Treaty (BT)	http://www.wipo.int/treaties/en/registration/pct http://www.wipo.int/treaties/en/registration/budapest
	Customer licensed to receive organism	National regulations	
	Dangerous organisms	EU Council Regulation No 1334/2000 of the 22 June 2000 setting up a Community regime for the control of exports of dual-use items and technology	http://europa.eu.int/eur-lex/en/consleg/pdf/2000/en_2000R1334_do_001.pdf#search='EU%20Council%20Regulation%20No%201334%2F2000'

BEST PRACTICE GUIDELINES ON HUMAN-DERIVED MATERIAL

1. Introduction

These domain specific best practice guidelines provide the basis for the best practices in the management of Biological Resource Centres (BRCs) that hold and supply human-derived materials.

In the post-genomics era, human-derived biological materials for basic research use in general and applied science constitute vital tools for clinical, health-related biotechnologies and the development of new pharmaceuticals, medical devices diagnostics and therapies.

It is widely recognised that BRCs that hold and supply authorised human-derived biological materials should do so in such a way as to provide a high quality service, consistent traceability (from the providers to the end-users) and appropriate transparency, in accordance with national and international legislation and regulations, as well as ethical commitments where these are required to apply.

These domain specific best practice guidelines assist BRCs to put into practice procedures that comply with relevant national law, regulations and policies. The best practice guidelines aim to provide a reliable basis for research and development in different laboratories and to contribute towards protection of the donor of human-derived biological materials in accordance with ethical principles, the health of laboratory personnel, the public and the environment.

Rules of ethics concerning the collection, use and safety of samples should be taken into account in the organisation and operation of any BRC so as to protect individuals as well as population groups.

2. Scope

These guidelines provide best practices that complement the document *General Best Practice Guidelines for BRCs*. They address the acquisition, maintenance and provision of human-derived biological material (see definition) by BRCs as well as the management of such BRCs.

BRCs dealing with human-derived biological material aim to assure the quality of such material, while ensuring that sensitive data are protected and that transactions between the various parties exchanging such material can be traced. BRCs should be organised in a manner that ensures the quality of the storage of biological material and provides for the correct and ethical use and distribution of the biological material. BRCs should adhere to internationally recognised ethical principles, particularly informed consent.

Bio-banks for therapeutic and diagnostic purposes are excluded from the scope of these best practice guidelines. The potential scientific value of collections that cannot meet these best practice guidelines should be recognised.

3. Definitions

These complement the definitions given in *General Best Practice Guidelines for BRCs*.

Human-derived biological material: For the purpose of these best practice guidelines, these are biological materials that are tissues, cells, cell lines and other human-derived components (as defined in *General Best Practice Guidelines for all BRCs*), and associated data (see definition), used for scientific research. Such biological material may be derived from individuals, families or population groups.

Collections: Assemblage, for research purposes, of biological material selected on the basis of clinical or biological characteristics

Associated data: Relevant information, using internationally recognised standards if possible, by which biological material can be identified and classified.

Donor: The individual from whom the biological material was derived.

Review board: Group of independent experts specialising in fields of, for example, science, medicine, ethics, data protection and protection of privacy etc.

Ethical Committee: A group nominated for the BRC or by the BRC or its host organisation able to draw upon appropriate fields of expertise, for example, related to issues of informed consent or intellectual property rights, relevant to ethical review.

Custodian: The person or legal entity initiating a collection.

User: Person authorised to use the biological material and/or associated data delivered by a BRC for scientific purposes.

Service: Work performed for a "client" (*e.g.* preparation, packaging, transport, duplication, storage, quality control, analysis), whether or not for a fee.

4. Organisational requirements

4.1. Compliance with law and ethics regulations

BRCs must comply with appropriate national and international laws, international rules and regulations and should follow the Ethical Committee's recommendations concerning use of human-derived biological materials and ethics.

In particular, human BRCs should respect laws and regulations in the areas of:

i) National certification of Biological Resource Centres, where such systems may be in place under the responsibility of national governments.

ii) Professional secrecy.

iii) Health and Safety (including Good Management Practice) or good manufacturing practice.

iv) Ownership of Intellectual Property Rights (IPR), when applicable.

v) Ethical matters, including, as appropriate, informed consent and respect for human dignity.

vi) Management of data bases and security of associated data.

vii) Employee safety.

viii) Environmental safety.

ix) Transport legislation, including import and export.

x) Classification of biological material on the basis of hazard (to take into account the actual or potential infectious status of human-derived biological material). In particular, BRCs should comply with (*Best Practice Guidelines on Biosecurity for BRCs*).

When engaged in activities related to the collection and use of human-derived material, BRCs should ensure:

xi) The preservation of the donor's dignity.

xii) The respect for the autonomy of the donor, particularly through informed consent, up to and including the possibility to withdraw his/her informed consent when samples and derived data have been stored in an identifiable manner.

xiii) The right of each individual to decide whether or not to be informed of the results of research if human-derived biological material is not anonymous.

xiv) The protection of the confidentiality of data stored or processed for research purposes.

xv) That the only samples included in a BRC are those for which enough material for potential future diagnostics and clinical purposes for the donor and/or his/her family, is available. Biological material collected without informed consent can, however, be distributed by BRCs so long as such actions have the approval of an ethical committee in accordance with national regulations.

4.2. Long-term sustainability

BRCs serve an invaluable function by acquiring, maintaining, and providing human-derived biological materials. BRCs should have procedures in place that comply with their host country's regulations and ethical provisions regarding human-derived biological materials, to ensure that their key holdings (biological material and data) remain available to those that need access to them.

4.3. Responsibilities of management

The BRC manager (see *General Best Practice Guidelines for BRCs*) should be qualified to make sound decisions, particularly on ethical, scientific and managerial issues. He/she should have the responsibility particularly to confirm:

i) The establishment of proper procedures for the sound operation of the BRC.

ii) The respect of ethical rules.

iii) The implementation and surveillance of quality control.

iv) The application of the decisions of the Review Board regarding control, access to and use of biological material.

v) The publication of general information on the activities of the BRC and research results obtained by using the biological material.

Many biological materials are initially collected for clinical purposes; their transfer into a BRC environment for research purposes and distribution need specific management (*e.g.* quality control, traceability, management of consent).

5. Staff - qualifications and training

5.1. Staff

Staff should have relevant qualifications, training and competence in human-derived biological material relevant to the scope of material held in the BRC.

All persons having access to a BRC should be bound by a duty of professional secrecy. Persons with access to confidential data should be contractually bound to medical secrecy obligations. Rights of access should be managed, traced and limited to authorised persons.

5.2. Training

All BRC staff should be briefed regularly and trained in the procedures in effect at the BRC. Training should be duly documented.

5.3. Hygiene and biosafety

Since human cells may be infected by pathogenic viruses or other micro-organisms, all staff should follow the procedures laid down under the appropriate level of containment for human-cells being handled, as defined by WHO's *Laboratory Biosafety Manual* and as interpreted by national law, regulations and policies, to avoid contaminating samples as well as to avoid the risk of infection.

BRCs should therefore institute procedures that ensure a suitable and sufficient assessment of the risks to health and safety to which any person whether employed by BRCs or not may be exposed through their work. Such procedures should be reviewed regularly, and changes to such procedures should be recorded.

All staff should follow the procedures laid down under the appropriate level of containments as defined by the World Health Organisation and as interpreted by national law, regulations and policies for micro-organisms that might be handled knowingly or inadvertently through the handling of human-derived biological material.

Important elements of a safe work place include:

i) Adequate assessment of risks.

ii) Provision of adequate control measures.

iii) Provision of health and safety information.

iv) Provision of appropriate training.

v) Provision of adequate individual protection devices.

vi) Establishment of records systems to allow safety audits to be carried out.

vii) Implementation of current best practices.

Best practice requires assurance that correct procedures are actually being followed and this requires a sound and accountable safety policy.

6. Premises

It is the responsibility of the BRC to provide an environment that is conducive to:

i) Handling aseptically human-derived biological material to prevent contamination during processing and facilitate accurate measurement and recording.

ii) Ensuring that dangerous organisms that could be misused are not distributed to unauthorised users, in accordance with national law (see *Best Practice Guidelines on Biosecurity for BRCs*).

iii) Assuming confidentiality of associated data.

iv) Providing site security.

7. Equipment use, calibration, testing and maintenance records

Cleaning, disinfection/sterilisation and maintenance of laboratory equipment should be performed by authorised and trained staff following documented procedures.

Special attention should be paid to the conditions for incubation and storage of biological material.

Appropriate maintenance and verification procedures for equipment in BRCs are summarised in Annex 1. The list does not apply to those BRCs that retain solely formalin-fixed material.

8. Documentation management

All documents should be readable and stored in a place where they can easily be located by authorised staff. They should be conserved in an environment which will avoid deterioration, fire damage, loss and/or tampering.

BRCs should use a data management system that includes a computerised inventory tracking system with appropriate security/data-access control safeguards.

All BRC procedures should be subject to documentary management throughout their lifetime.

All movements into or out of the collection of biological material should be documented.

Often, human BRCs require that stored biological material be linkable to the personal genealogical and clinical data of the donor. It is imperative that security and confidentiality are respected to address privacy issues. Any documentation on biomedical data should be kept in secure cabinets accessible only to authorised personnel.

The documentation managed by databases should be saved, secured and duplicated in a different site.

BRCs should develop a disaster plan which includes appropriate privacy protection for personal information and equipment.

9. Informatics

9.1. Data

BRCs should ensure a minimum amount of information is available for each accession in the collection (the Minimum Data Set (MDS)). Additional data may comprise a Recommended Data Set (RDS). Best practice for what should comprise each data set is listed in Appendix 2. The MDS should be recorded and made available.

The data should be updated with the most recent information related to donor's sample (*i.e.* clinical data, results of scientific research).

Exceptionally, BRCs may accept collections of scientific value that cannot meet the full MDS and should disclose which items of the MDS are missing.

The data vocabulary used for the BRC catalogue should be in accordance with an identified thesaurus (*e.g.* Online Mendelian Inheritance in Man).

A procedure for defining the MDS and RDS for a collection should be established before the collection is constituted.

BRCs should be equipped with information systems that can handle physical management of samples. This implies a system that records data on all stages of handling from sampling to transfer of all or part of a collection. There should be traceability of analyses undertaken, as well as of quality controls and transformations.

Identifying (associated) data may be recorded and transmitted securely, *e.g.* by e-mail or over the Web, only in accordance with the applicable regulations.

Donor identities should be encrypted in databases. The procedure for coding biological material is paramount to the protection of the donor's privacy as well as for allowing distribution and use for research purposes.[14]

9.2. Security of data

In order to guarantee security, BRCs should use a specific database for storing the personal data of the donor, never available to outsiders. Such data should be updated as additional information related to donors become available.

14 . See section 8.3 Access to Data and Publication of *General Best Practice Guidelines for all BRCs.*

Data should be saved reasonably regularly in order to avoid data loss.

9.3. Internet publication

The BRC should publish a catalogue of human-derived biological material accessible in order to:

i) Optimise the utilisation of biological material.

ii) Ensure transparency of BRC activities.

A catalogue should contain the list of available samples associated with a synopsis of the minimum data set (see Appendix 2) and the conditions for access.

Prior to publication, sufficient means should be taken to ensure that no individual can be identified from the information provided.

10. Services of BRCs

BRCs may engage in research and development activities relevant to their missions.

BRCs may provide services in accordance with ethical and legal regulations.

BRC should take reasonable steps to ensure that services from an outside provider are rendered in accordance with the regulations and good practices in force in the appropriate field, that are applicable in the jurisdiction relevant to the BRC as well as in the jurisdiction relevant to where the service is to be performed.

Inflows and outflows of biological material should be recorded, and when it is necessary to transport samples, their transport should be documented and carried out in compliance with the applicable standards and regulations.

11. Preparation of samples

Accurate preparation is one of the fundamental steps in the maintenance of biological material and should be given special attention.

Sample preparation techniques should be stipulated in procedures and operating instructions that should be validated and revised periodically.

BRCs should have documented standards and procedures for all preparations. There should also be written procedures for updating, approving and adopting all documents.

Consumable material used should be of a high standard.

12. Accession of deposits to the BRC

12.1. Receipt and handling of biological material

BRCs should implement safe, documented procedures for the receipt and storage of human-derived biological material that are appropriate to the hazard posed by such material. All incoming parcels that contain unknown or hazardous biological material should be opened in a suitable containment laboratory or appropriate microbiological safety cabinet with local facilities

for the safe handling and disposal of biological material. Safety procedures should be laid down and documented.

Conditions of deposit should be determined and agreed upon, if pertinent, in a material transfer agreement (MTA). Where deposits are outside the remit of a BRC, suitable BRCs should be recommended.

The depositor should provide proof that prior informed consent to collect and deposit the primary human-derived biological material in a BRC has been obtained or reasonable efforts have been taken to obtain such consent (with proof of ethical review).

On deposit of human-derived biological material, BRCs should record ownership and terms and conditions for further distribution.

A unique identification number should be allocated to the biological material, which should never be reassigned to other material even if the original biological material is later discarded.

In any situation in which a BRC has in its possession information that could identify a donor, such information should be dissociated from the biological material concerned and any other associated data.

Specific care should be taken to ensure that data in the possession of a BRC is not misused in such a way as to cause harm to individuals or groups of individuals.

12.2. Accession

52. The biological material received should be accompanied by information required by the individual BRC.

12.3. Quality checks on biological material

BRCs should institute a system of quality control that monitors the process of preparation and conservation of samples received. Such a system should also ensure the quality of the minimum data set generated for each sample received. The quality control methodologies used should reflect the differing nature of the biological material received (see Appendix 3). In each case, specific quality control procedures should be laid down and followed.

When validating the quality of human-derived biological material for specific research applications, BRCs should strive to use as little of the biological material as possible.

13. Preservation

For each type of human-derived biological material, appropriate preservation method(s) should be chosen by the BRC based on its own experience or on the recommendations of the depositor (examples of technical preservation of applicable material are given in Appendix 4).

BRCs should avoid unnecessary thawing and refreezing of frozen biological material. Checks should be in place to assure and validate storage stability.

A written procedure should be available for the preservation of samples by each available means of storage.

Storage conditions should ensure that loss of material is prevented. Where applicable:

i) Storage temperatures should be monitored continuously, and incidents and alarms should be documented and traceable, in relation to the biological material involved.

ii) The freezer container should be equipped with an alarm system that ensures an immediate intervention, 24 hours a day, all year round.

iii) Procedures for transfer in the event of a breakdown should be defined, including the obligations of staff.

An empty functioning freezer should be available in case of single freezer failure.

Validation of the methods and procedures used for preservation should be carried out to ensure their reproducibility and reliability by using one of the following approaches:

i) Performing blind tests.

ii) Calibration.

iii) Comparing the results of the same method performed at different times.

iv) Comparing results obtained with different methods.

v) Comparing the results obtained for the same method performed by different persons.

vi) Participation in relevant ring trials.

The results of the validation of methods and procedures should be recorded.

Where possible, duplicate samples should be made and stored as a duplicate collection at a separate location.

14. Supply of biological material

14.1. Order placement

BRCs should supply biological material to other BRCs and public or private institutions for research purposes only.

BRCs should pay specific attention to the authentication of new clients (first orders from new clients should be received on an order form with the client's official letterhead and signed by an authorised person) and of their individual representative(s). BRCs should provide an appropriate and protected follow-up mechanism to maintain adequate authentication.

A material transfer agreement, if pertinent, should be drawn up between the BRC and the user so the user can be informed of his/her rights and duties relating to the biological material or the collection requested (for example, relating to intellectual property rights, consent, publication, result reporting requirements, quoting BRC accession numbers in publication).

BRCs should ensure that an appropriate review board has considered and approved proposed research topics prior to releasing human-derived biological material for such purposes.

An order should only be accepted when the required accompanying documentation is completed, signed and returned.

BRCs should conduct their operations in accordance with the *Best Practice Guidelines on Biosecurity for BRCs*.

14.2. Availability of the biological material ordered

Human-derived biological material should be dispatched, where practicable, as soon as possible once necessary licenses and/or documentation are provided.

With biological material of Risk Group 2 (*WHO Biosafety manual*, 2004) and higher the BRC should have written and signed documentation proving the user has the appropriate authorisation to import and handle such biological material.

BRCs should seek to serve the interests of the wider scientific community, in that material should be made available to a broad scientific community for use in high quality research.

BRCs should develop a distribution strategy that addresses how they will manage possible conflicts between hold and supply activities in cases of rare and/or precious samples as well as for those samples that cannot be replenished.

If a biological material cannot be immediately delivered, the BRC should inform the user of an estimated date of supply.

14.3. Information provided with the biological material supplied

The BRC should at least provide to the user:

i) A minimum data set according to the type of resource (See Appendix 2)

ii) The repository conditions needed to maintain the biological material (temperature, medium, culture conditions etc.).

iii) The transportation conditions.

iv) A safety data sheet in the case of a material containing a hazardous organism or its derivative, including the containment level required for handling the biological material, disposal measures and measures to take in case of spillage. Human cells, tissues should always be treated as hazardous unless they are tested for infectious diseases or treated with an appropriate inactivation measure (*e.g*. fixation with formaldehyde). The safety data sheet should be mandatory for any dangerous material and should be included in the package, together with instructions for handling.

In circumstances in which information is supplied that pertains to a donors' identity, such information should be encrypted (type of code depending on procedures previously determined).

14.4. Packaging

The packaging of biological material and its transport by postal and other transport services are covered by international and regional agreements and national laws (see Appendix 6). The BRC

should ensure that any changes to applicable legislation and regulations are implemented in their procedures.

Packages of the human-derived biological material should be labelled according to international rules and have the appropriate customs declaration, biological hazard label and import/export permit where appropriate.

Human-derived biological material, not known to be infectious and derived from a normal risk population may be sent by (air) mail or other means of transport according to the Universal Postal Union (UPU) requirements (see Appendix 6).

A BRC should ensure that staff responsible for the distribution of infectious substances via air have the required shipper training certificate.

15. Quality Audit and Quality Review

Internal and external audits are necessary to monitor quality (focus on developing preventative actions and maintenance), and should be performed regularly and duly documented.

Quality review should be built into the procurement, processing, testing, storage and delivery of material.

APPENDIX 1 – EXAMPLE INVENTORY OF BRC EQUIPMENT AND ITS MAINTENANCE AND CALIBRATION

Item	*Maintenance required*	*Calibration*
Autoclave	Cleaning, pressure vessel maintenance contract; Run with indicators	Manufacturer's service
Incubator	Cleaning, system of surveillance, Maintenance contract	Manufacturer's standard on service, temperature calibration
Liquid Nitrogen storage vessels	Clean, leakage, pressure, temperature check	Five yearly Manufacturers' Test
Centrifuge	Clean	Regular cleaning; Manufacturer's service
Cryo-storage tanks	Removal of condensation and ice Look for malfunction of Liquid nitrogen level alarms	
Liquid Nitrogen store oxygen level alarm	Maintenance contract	Manufacturer's standard on service
Programmed Cooler	Maintenance contract	None
Cryomicrotome	Clean after use Temperature calibration	Calibration equipment provided for test at each time of use
Microtome	Clean after use	
Microscope	Clean after use	Annual Functionality test
Laminar Flow Cabinet	Clean after use, Airflow check Particle count	
Class II Microbiological Safety Cabinet	Maintenance contract, Particle count KI test	Manufacturer's standard on service
DNA Extractor	Clean after use	Manufacturer's standard on service
-80°C freezer	Temperature check Clean	Manufacturer's service, temperature calibration
-20°C Freezer	Temperature check	temperature calibration
Media preparation equipment		
Balance	Clean after use Maintenance contract	Manufacturer's standard on service
pH meter	Clean after use	Test against Manufacturer's standard
Computer	Firewall, safeguard,	

APPENDIX 2 – A MINIMUM (MDS) AND RECOMMENDED (RDS) DATA SET[15]

Data set for DNA

MDS (data without asterisks should be provided to users)	RDS
- **Identification of depositor*** - **Identification number of the family*** - **Identification number of the donor*** - Identification number of the biological material - Consent/approval by ethical committee (Y/N) - Gender and age of donor - Pathology of family with OMIM[1] number - Status of the biological material (*e.g*. affected, non-affected, indication of suspected diagnosis). - Date, year and month of the collect of the material. - Nature of the human biological material where DNA was extracted from (*e.g*. affected, non-affected). - Preservation or storage conditions - Quantity of biological material: – for DNA : concentration µg/µl and number of µl	- Consent - Family tree - Samples from relatives available - Form of supply - Maximum delay for delivery (linked to the nature of a given biological material) - Karyotype - Quantity of families and subjects available for the specific disease - Detail information of treatment/medications - Information on disease outcome -Associated clinical data (*e.g*. laboratory parameters, imaging data, molecular data) -Information on life style - Information on family history - DNA fingerprinting or another method of authentication - Hazard status

1. OMIM™ (Online Mendelian Inheritance in Man™) - A database which represents a catalogue of human genes and genetic disorders

Data set for tissues and isolated cells

MDS (data without asterisks should be provided to users)	RDS
- **Identification of depositor*** - **Identification number of the donor*** - Identification number of the biological material. - Consent/approval by ethical committee - Gender and age of the donor - Disease diagnosis - Status of the biological material (*e.g*. affected, non-affected, indication of suspected diagnosis, indication of grade of tumor). - Origin of the biological material (organ and tissue) - Date, year and month of the collect of the biological material. - Hazard status - Nature of the human biological material (*e.g*. tissue, slide, cells, pellet) - Documentation on processing method (*e. g*. chemical preservation) - Preservation or storage conditions (liquid nitrogen, -80°C, room temperature)	- Consent - Details of diagnosis - Related biological material (DNA, biopsy) - Quantity or concentration available - Characteristics of the sample (*e.g*. sample composition, content tumour cells) - Delay of freezing - Form of supply - Maximum delay for delivery (linked to nature of the biological material) - Information on treatment/medications - Information on disease outcome - Associated clinical data (*e.g*. laboratory parameters, imaging data, molecular data) - Information on life style - Information on family history - DNA fingerprinting or another method of authentication

15 . According to the type of resource.

Data set for cell cultures (cell line, primary cultured cells and transformed cells)

MDS	RDS
- Identification of depositor - Identification number of the biological material. - Gender and age of donor - Disease diagnosis - Type of cell line (cell line, primary cultured cells, transformed cells). - Origin of the biological material (organ and tissue) - Date, year and month of the collect of the material. - Hazard status - Nature of the cells (*e.g.* epithelia, fibroblast, lymphocyte). - Culture condition (medium and subculture routine) - Preservation or storage conditions	- Consent - Details of diagnosis and outcome of disease - Characterization of cells (doubling time, tumorigenicity, karyotype etc.) - Related biological material (tissue, serum, DNA) - Quantity or concentration available - Number of passage - Form of supply - Maximum delay for delivery (linked to nature of the biological material) - Detail information of treatment - Morphology and growth characteristics - Reference paper (for cell lines) - DNA fingerprinting or another method of authentication

APPENDIX 3 – RECOMMENDED QUALITY CONTROL PROCEDURES

DNA quality controls

Check DNA concentration by OD at 260nm
Check purity of DNA by OD260 /OD280 ratio
Check the integrity of DNA by agarose gel electrophoresis

Tissues and isolated cells controls

Check tissues for quality of fixation and sample composition by microscopic studies
Check the cells by morphological and biological studies
Check quality of the frozen samples yearly, by extracting and analysing DNA and RNA

Cell cultures controls

Check growth on appropriate medium
Check contamination from mycoplasma, bacteria, fungi and virus
All chromosomally aberrant cell cultures, human/rodent somatic cell hybrid cultures, and normal controls are karyotyped by G-banded analysis
Authenticate cell line by appropriate tests (PCR, immuno-phenotypic tests, microsatelite tests).

APPENDIX 4 – RECOMMENDED PRESERVATION METHODS

General

Choose storage vessel in accordance with storage conditions and size of biological material; choose labelling and printing systems that will be stable under the long term storage conditions

DNA preservation

Conservation in –20°C container or lower temperature
Freeze drying

Tissue

Paraffin embedded samples, conservation at room temperature (below 27°C)
Cryopreservation of samples, storage in –80°C freezers or liquid nitrogen (liquid or gas phase)

Isolated cells

cryopreservation in or above liquid nitrogen or in ultra low temperature (-150°C) freezer
cryopreservation in –80°C C container only for short periods

Cell lines

cryopreservation in freeze medium (containing cryoprotectant like Dimethyl sulfoxide), in or above liquid nitrogen or in ultra low temperature (-150°C)

APPENDIX 5 – SUMMARY OF KEY ELEMENTS OF NATIONAL AND INTERNATIONAL REGULATORY CONTROLS POSTING TO HUMAN DOMAIN BRCS

Ethical principles

Nuremberg Code, 1947. http://www.cirp.org/library/ethics/nuremberg/

Universal Declaration on the Human Genome and Human Rights, UNESCO, 11 November 1997. http://www.unesco.org

Declaration of Helsinki (1964) of the World Medical Association (WMA) and its subsequent Declarations of Tokyo (1975), Venice (1983) and Hong Kong (1989) have further defined the framework for biomedical research in the human patient http://www.wma.net/e/index.htm

Belmont report: ethical principles and guidelines for the protection of human subjects of research (1998). http://ohsr.od.nih.gov/guidelines/belmont.html

EUROGAPPP Project 1999-2000,. Data Storage and DNA banking for biomedical research: informed consent, confidentiality, quality issues, ownership, return of benefits – A professional Perspective. European Society of Human Genetics Public and Professional Policy Committee, 30 October 2000, http://www.eshg.org

Human tissue: ethical and legal issues, Nuffield Council on Bioethics, 1995
http://www.nuffield.org/bioethics/publication/pub0006740.htm

The use of human biological materials in research: ethical issues and policy guidance. National Bioethics Advisory Commission, 3 December 1998.
http://onlineethics.org/reseth/nbac/hsummary.html

Opinion No. 11 of the European Group on Ethics in Science and New Technologies to the European Commission on Ethical Aspects of Human Tissue Banking.

Proposed international guidelines on ethical issues in medical genetics services. World Health Organization, 1998. http://www1.umn.edu/humanrts/instree/guidelineproposal.html

Opinion of the German National Ethics Council on Biobanks for Research
http://www.ethikrat.net/_english/publications/Opinion_Biobanks-for-research.pdf

Convention for the protection of Human Rights and dignity of the human being with regard to the application of biology and medicine: Convention on Human Rights and Biomedicine (Oviedo, 4.IV.1997) (Council of Europe, European Treaty Series, No. 164). http://casi.org.nz/statements/decbiomedicine.html

Informatics

International declaration of human genetic data, 2003 – UNESCO
http://portal.unesco.org/shs/en/ev.php-URL_ID=1882&URL_DO=DO_TOPIC&URL_SECTION=201.html

APPENDIX 6 – WEBSITES OF INTEREST FOR INFORMATION

Biodiversity

Convention on Biological Diversity: http://www.unep.org/biodiv.html

International Organisations

World Federation for Culture Collections: http://www.wfcc.info/

World Data Centre for Micro-organisms: http://wdcm.nig.ac.jp/

Common Access to Biological Resources and Information: http://www.cabri.org

European Biological Resource Centres Network: http://www.ebrcn.org

ASM – Asian Consortium for the Conservation and Sustainable Use of Micro-organisms http://www.abrcn;net

ECCO, European Culture Collection Organisation: http://www.eccosite.org

Food and Agriculture Organization (FAO): http://www.fao.org/

World Animal Health Organization (OIE): http://www.oie.int/eng/en_index.htm

International Plant Protection Convention (IPPC): https://www.ippc.int/IPP/En/default.jsp

International Police Organization (INTERPOL): http://www.interpol.int/

The Australia Group: http://www.australiagroup.net/

Biological Weapons Convention (BWC): http://disarmament.un.org/wmd/bwc./

MIRCEN Scholarships: http://portal.unesco.org/sc_nat/

UNESCO People, Biodiversity and Ecology http://www.unesco.org/mab/index.shtml

WIPO - World Intellectual Property Organization : http://www.wipo.int

ISO - International Organization for Standardization: http://www.iso.ch/iso/en

Patents

Budapest Treaty on the International recognition of the Deposit of Micro-organisms: http://www.wipo.int/treaties/en/registration/budapest/

Transport and shipping

First generation guidelines for NCI-Supported Biorepositories – Federal register Vol. 71, Number 82, Page 25814, April 28, 2006.	http://biospecimens.cancer.gov/biorepositories/guidelines_full_formatted.asp
International Laboratory Accreditation Cooperation (ILAC)	http://www.ilac.org/
Micro-Organisms Sustainable use and Access regulation International Code of Conduct	www.belspo.be/bccm/mosaicc
CABRI Guidelines	http://www.cabri.org/gidelines.html
Canadian Transport	www.rural-gc.agr.ca/e4.1_canutec.html
European Commission DGVII – Transport	http://europa.en.int/en/comm/dg07/index.htm
Harmonisation of UN documents etc.	www.hazmat.dot.gov/rules
International Air Transport Association	www.IATA.org/cargo/dg www.IATA.org/cargo/dg/links.htm
International Civil Aviation Authority	http://hazmat.dot.gov/icao.htm www.volpe.dot.gov/ohm/icao.htm www.cam.org/~icao/menu3.html
Maritime rules	www.eat.co.uk/ncec/complian/bibliog/bysea.html www.mdnautical.com/imo/cargoes.htm www.imo.org/pubs/pubcats.htm www.info.gov.hk/mardep/notices/mdn98149.htm www.hazmathelp.com/imdg.htm
The European Agreements Concerning the International Carriage of Dangerous Goods by Rail (RID) and by Road (ADR)	http://hazmat.dot.gov/RIDADR.htm www.dsidat.com/products/undisk7.htm www.volpe.dot.gov/ohm/ridadr.htm
Transport – general German magazine	www.tci-transport.fr www.hazmathelp.com/dotlink.htm www.cefic.org www.storck-verlag.com/english/gela_e.htm
United Nations meetings agenda and minutes	www.unece.org/unece/trans/danger/meetdoc.htm
UN Model Regulations	www.unece.org/unece/trans/main/dgdemo/intro.htm
UN Committee of Experts	www.tc.gc.ca/tdgoods/consult/unlinks_e.htm
Universal Postal Union	http://ibis.ib.upu.org http://unicc/unece/tra www.de/facil/upustr.htm
USA Dept of Transport's Office of Hazardous Materials Management	http://hazmat.dot.gov
WHO Guidance on Regulations for the Transport on Infectious Substances	http://www.who.int/csr/resources/publications/biosafety/WHO_CDS_CSR_LYO_2005_22/en/

Hygiene and Bio-safety	
Organisation for Economic Co-operation and Development (OECD)	http://www.oecd.org/dataoecd/4/4/34932656.pdf
United Nations Industrial Development Organisation (UNIDO) Bio-safety Information Network and Advisory Service (BINAS)	www.who.org/emc/biosafe/index.htm
International Centre for Genetic Engineering and Biotechnology (ICGEB)	www.aphisweb.aphis.usda.gov.biotech
US Animal and Plant Health Inspection Service (APHIS)	www.nal.usda.gov/bic/
US Food and Drug Administration (FDA)	http://www.fda.gov/
World Health Organization (WHO) Biosafety Programme	http://www.who.int/csr/labepidemiology/projects/biosafetymain/en/index.html
U.S. Departments of Health and Human Services (HHS) and Agriculture (USDA) rules implementing USA PATRIOT Act and Public Health Security and Bioterrorism Preparedness and Response Act of 2002	http://www.cdc.gov/od/sap/final_rule.htm
Centre for Food Safety and Applied Nutrition (CFSAN)	http://vm.cfsan.fda.gov/list.html
Belgian Bio-safety Server	www.biosafety.be
The Dutch Genetically Modified Organism Bureau	www.rivm.nl/csr/bggo.html
Biotechnology Information Centre (BIC) of the US Department of Agriculture (USDA)	www.nal.usda.gov/bic/
UK Advisory Committee on Releases into the Environment (ACRE)	www.environment.detr.gov.uk/acre/index.htm
National Chemical Emergency Response UK	www.eat.co.uk/ncec/complian/bibliog/bibliog.htm
American Biological Safety Association (ABSA)	http://www.absa.org
European Biosafety Association (EBSA)	http://www.ebsaweb.eu
International Biosafety Working Group (IBWG)	http://www.internationalbiosafety.org/english/index.asp
Advisory Committee on Dangerous Pathogens	http://www.doh.gov.uk/bioinfo.htm

Useful bibliography

Anon (1994). Approved Code of Practice for Biological Agents 1994. Health and Safety Executive. Sudbury: HSE Books.

Anon (1996b). European Standard EN 829:1996 E: Transport packages for medical and biological specimens, Requirements, tests. Brussels: CEN, European Committee for Standardisation.

Cartagena Protocol on Biosafety to the Convention on Biological Diversity, http://www.biodiv.org/doc/legal/cartagena-protocol-en.pdf

EC Council Directive 2000/29/EEC on protective measures against the introduction into the Member States of harmful organisms of plant or plant products. OJ No. L. 169, p.1 of 10.07.2000

EC Council Regulation 1504/2004 amending and updating Regulation 1334/2000

EC Council Directive 95/44/EC on establishing the conditions under which certain harmful organisms, plants, plant products and other objects listed in Annexes I to V to Council Directive 77/93/EEC may be introduced into or moved within the Community or certain protected zones thereof, for trial or scientific purposes and for work on varietal selections

EC Council Directives 90/219/EEC and 98/81/EC on contained use of genetically modified organisms

EC regulation 1946/2003 on the transboundary movement of genetically modified organisms (pertains to Cartagena Protocol on Biosafety)

EC Council Directive 2000/54/EEC On the protection of workers from risks related to exposure to biological agents at work. OJ No. L. 262, pp.21-45 of 18.09.2000

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POSSIBLE APPROACH TO NATIONAL CERTIFICATION

Introduction

BRCs retain collections of biological material and associated information to facilitate access to biological resources and to ensure that they remain available for sustainable use.

Box 1. OECD definition of Biological Resource Centres

"Biological Resource Centres are an essential part of the infrastructure underpinning biotechnology. They consist of service providers and repositories of the living cells, genomes of organisms, 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. BRC 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 collections are entities compliant with appropriate national law and regulations, and have been constituted to fulfil many crucial roles, which include:

- Preservation and supply of biological resources for scientific, industrial, agricultural, environmental and medical R&D and biotechnological processes.
- 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.

This document provides a sample of an approach that could be used by some countries, should they choose to establish a certification process for BRCs.

To become a certified BRC, a certification process through independent review by a third party to prove compliance with OECD's "Guidance for the Operation of Biological Resource Centres (BRCs)" should be successfully performed.

General BRC certification rules

Certification bodies should be acknowledged by national governments either through an accredited certification body recognised by government or through a transparent certification procedure recognised by government or directly by government.

Governments would be responsible for ensuring that their respective certification body is independent, qualified and has no conflict of interest with the BRC seeking certification (see Notes).

Certification could be based upon implementation of the applicable operative OECD best practices[16].

Future revision of these best practice guidelines could be negotiated and approved by the community of certified BRCs.

Certification mechanism

Any certification process and resultant requirements for certification bodies and third party auditors should be according to international standards as described in Notes.

General criteria for certified BRCs

A national certification procedure would likely require certified BRCs to comply with:

- Their national legislation, regulations and policies concerning acquisition, conservation, utilisation, including the fair and equitable sharing of benefits arising from utilisation of genetic resources, and distribution of biological resources and data related thereto.
- The regulations of the relevant countries when moving biological materials across national boundaries.
- The relevant national and international agreements, regulations, policies, frameworks and recommendations.

Certified BRCs should have in place a mechanism that updates their knowledge of the above (see the preceding paragraph).

When certification is granted it should indicate the highest level of hazard, where appropriate, that the BRC is qualified to handle.

16. Biological Resource Centres comprise several sets of guidelines that together provide the basis for best practices in the management of BRCs. Two sets of general best practices guidelines address all Biological Resource Centres, no matter what type of biological material they hold and supply. These are: *General Best Practice Guidelines for all BRCs* and it is supplemented by *Best Practice Guidelines on Biosecurity for BRCs*. Further guidelines provide additional best practices for those BRCs that hold and supply biological material within specific domains. Best practice is achieved when BRCs comply with all sets of general guidelines applicable to the specific domain that the biological materials they hold and supply belong to.

NOTES

1. Requirements for certification bodies and third party auditors

A certification body would need to meet the following requirements:

- The certification body shall be accredited in accordance with ISO 17021([17]) through accreditation body signatory of an international multilateral recognition agreement (*e.g.* International Accreditation Forum).
- The certification body demonstrates its capability and experience in biotechnology (*e.g.* accreditation in EAC scopes 35/38).[18]
- The certification body demonstrates the availability of qualified and experienced auditors.

The auditors would need to fulfil the following requirements:

- Qualification as ISO 9001 auditors.
- Practical work and auditing experience in biological laboratories or biotechnology.

2. Certification process

Any certification process would need to be in line with requirements laid down in ISO 17021 and ISO 19011.[19]

In addition to the items laid down in ISO 17021, the certificate should indicate:

- The scope with the highest level of hazard the BRC is qualified to handle.
- The OECD reference guidance.

3. Audit criteria

In addition to the criteria laid down in ISO 19011, the audit would need to cover (where applicable) the following chapters, as set out in Part II of the OECD Best Practice Guidelines for BRCs:

- Guidance for the Operation of Biological Resource Centres (BRCs): *General Best Practice Guidelines for all BRCs.*
- Guidance for the Operation of Biological Resource Centres (BRCs): *Best Practice Guidelines on Biosecurity for BRCs.*
- Guidance for the operation of Biological Resource Centres: *Best Practice Guidelines for the Micro-organism Domain.*
- Guidance for the operation of Biological Resource Centres: *Best Practice Guidelines for Human-derived Material.*

17. ISO/IEC 17021:2006. Conformity assessment -- Requirements for bodies providing audit and certification of management systems".
18. The scopes of Quality Management System accreditation is based on the statistical nomenclature for economic activities published by European co-operation for Accreditation. Code EAC 35 = Other services, Code EAC 38 = Health and social work.
19. ISO 19011:2002 "Guidelines for Quality and/or Environmental Management Systems Auditing".

ANNEX I

List of countries actively participating in the Task Force on Biological Resource Centres established by the OECD's Working Party on Biotechnology.

OECD Members	OECD observer countries	Invited Experts	Other Organisations
Australia	China	Brazil	UNESCO
Austria	Russian Federation	Burkina Faso	UNIDO
Belgium	South Africa	Colombia	
Canada		India	
Czech Republic		Laos PDR	
France		Malaysia	
Germany		Philippines	
Italy		Senegal	
Japan		Thailand	
Korea			
Netherlands			
Portugal			
Spain			
United Kingdom			
United States			

ANNEX II

Methodology used for the pilot study on best practices for Biological Resource Centres (BRCs)

The pilot study performed on the best practices for BRCs and mentioned in the Part I of the report consisted of four distinct elements as follows:

i. Broad public consultation on the OECD best practice guidelines for BRCs

Broad public consultation sought comments from a broad range of stakeholders on practicality, implementation and technical accuracy of best practices for BRCs. Three sets of best practices were sent for comments to around 500 stakeholders:

a) Possible National Approaches to Certification.

b) General Best Practice Guidelines for All BRCs.

c) Best Practice Guidelines for the Micro-Organism Domain.

The comments received were gathered together and presented to participants in the pilot study at a debriefing workshop (see item ***iv*** below) for consideration and further amendment of best practices.

ii. Briefing meeting on "Goals and methodology for the pilot study" held on 5-6 September 2006, Braunschweig, DSMZ, Germany

Twelve culture collections from OECD member and non-member countries and three certification/accreditation agencies participated. The meeting aimed to provide culture collections and accreditation/certification agencies with guidance on how to perform the desk top exercise element of the pilot study and on the expected achievements from this. Participants in the meeting agreed on the proposed methodology and time frame for delivery of the desk top exercise.

iii. Desk top exercise

Each participating body assessed the practicality and impact of the draft operational guidance for BRCs within their own facilities, in accordance with the methodologies and goals agreed at a briefing meeting on 5-6 September 2006. Short written reports from each participating body describing key conclusions and suggesting changes to the documents were submitted to the Secretariat by the end of the desk top exercise. The OECD Secretariat together with small group of experts gathered the reports together and amended the documents in accordance with the comments received. The revised versions of best practices together with

comments received were then presented at the debriefing workshop held in November 2006 for consideration and agreement (see item ***iv*** below).

iv. Debriefing workshop on the "Pilot study on operational guidance for BRCs" held on 14-15 November 2006, Brussels, BCCM, Belgium

The workshop aimed to analyse experiences of participants in the pilot study and to amend best practices for BRCs in light of such experience. All comments raised from the broader public consultation and the desk top exercise have been dealt with adequately. The amended and agreed by participants in the pilot study best practices were presented to the final meeting of the TFBRC on 4-5 December 2006 for agreement by the participants in the expert Task Force.

ANNEX III

ASSESSMENT OF COSTS ASSOCIATED WITH IMPLEMENTATION OF THE OECD BEST PRACTICE GUIDELINES FOR BRCS
CHINA

China General Microbiological Culture Collection (CGMCC) of the Institute of Microbiology, Chinese Academy of Sciences was built in 1951, and is now the largest culture collection in China. It deals primarily with bacterial and fungal cultures. CGMCC is a national depository for patent strains since 1985, and an International Depository Authority (IDA) under the regulations of the Budapest Treaty since 1995. At present, it has more than 14.500 strains of bacteria, yeasts and filamentous fungi which are maintained. CGMCC is a nonprofit organization financed by the Chinese Government.

Estimation of Time

1. November 2006 to March 2007

   Set up the Quality and Environmental Management System, including Quality and Environmental Management Manual, Standard Operating Procedures (SOPs), all the documents needed, and the record systems (forms/charts).

2. April 2007

   Training: Ensure all staff members know the policies and what more are required to do on quality matters.

3. May 2007 to July 2007

   Implementation and try running the entity according to the newly established Quality and Environmental Management System.

4. August 2007

   Internal audit

5. September 2007

   Fault rectification

6. October 2007

   Application to CQC for the certification

Cost Analysis

The table below presents estimated costs related to compliance with best practices for BRCs:

Estimation of Costs

Item	Costs (EURO€)
Cultures duplicate storage	15 000
Personnel (3)	23 000
External audit	12 000
Other direct costs	5 000
Total	**55 000**

ITALY

The Banca Cellule e Colture in GMP (ICLC) is a core facility of the "National Institute for cancer Research of Genoa". It was set up in 1994 and offers a service of storage, quality control and distribution of certified human and animal cell lines. ICLC is conducted by five people, one MD and four PhD in biology, two of which on a temporary basis.

Cost Analysis

The table below presents estimated costs related to compliance with best practices for BRCs:

Cost analysis for complying

Item	Costs (EURO €)
One technician (IST contract)	22 000
One secretary	18 000
Periodical external audits	5 000
Equipment	30 000
Total	**75 000**

THE NETHERLANDS

The Centraalbureau voor Schimmelcultures (CBS) - an institute of the "Royal Netherlands Academy of Arts and Sciences" (KNAW) and situated in Utrecht - maintains a collection of living filamentous fungi, yeasts and bacteria. The Institute's research programs principally focus on the taxonomy and evolution of fungi as well as on functional aspects of fungal biology and ecology, increasingly making use of molecular and genomics approaches. The institute employs circa 50 personnel, among whom 17 scientists.

Cost Analysis

The table below presents estimated costs related to compliance with best practices for BRCs:

Cost analysis for CBS to become a BRC

Item	Costs (EURO €)
Initial costs *Advisor / Trainer*	35 000
Continuously miscellaneous costs *Audits* *Evaluation Customer Satisfaction* *5% additional workload for staff* *Consultation*	75 000
Total 1st year	**110 000**
Total subsequent years	**75 000**

GERMANY

The DSMZ (Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH / German Collection of Microorganisms and Cell Cultures Ltd.) collections contain more than 19.000 microorganisms, 1.200 plant viruses and sera, 600 human and animal cell lines, 700 plant cell cultures and more than 7.200 cultures deposited for the purposes of patenting and safe deposit. The DSMZ is an independent, non-profit organization with approx. 100 personnel, thereof 40 scientists.

Cost Analysis

As the costs of implementing the OECD-BRC Best practice guidelines are comparable with the costs for implementing ISO 9001, the cost analysis for DSMZ is based on this financial analysis:

Item	Costs (EURO €)
Initial costs	80 000
Consulting	*55 000*
Equipment maintenance	*8 000*
Laboratory adjustment	*10 000*
External Audit	*7 000*
Continuously miscellaneous costs	101 000
Audits	*5 000*
Evaluation customer satisfaction	*1 000*
Quality Manager	*65 000*
Additional workload for staff	*15 000*
Equipment and laboratory maintenance	*15 000*
Total 1st year	**96 000**
Total subsequent years	**101 000**

Time Analysis

The preparations for the ISO 9001 certification for the branches micro-organisms, plant cell cultures, plant viruses and human and animal cell cultures required 10 months. The same timeframe could be expected for the implementation of the OECD best practice guidelines for BRCs.