Networking collections to provide facilitated and legislation compliant access to microbial resources

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INTRODUCTION

The Global Biological Resource Centre Network (GBRCN) Demonstration Project emanates from an Organisation for Economic Cooperation and Development (OECD) Working Party on Biotechnology initiative and the Task Force on Biological Resource Centres (BRC). Discussions began at a workshop in Tokyo in 1999 which was followed by a report in 2001 (OECD 2001) recommending efforts to address sustainability of BRCs and their better involvement in biotechnology. Subsequent activity culminated in the publication of the best practice guidelines for BRCs (OECD 2007). The final OECD BRC workshop recommended a demonstration project as a proof of concept for the establishment of the GBRCN. A small central Secretariat was supported by the German Ministry of Research and Education (BMBF) to co-ordinate activities to deliver the tools that could establish this global network. The project was established at the end of 2008 and funding ran to the end of November 2011. The Secretariat continues its operations for the moment without BMBF funding through commitments made by CABI and the Leibniz-Institut DSMZ - Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH. The overall goal of the GBRCN is to provide improved resources for the life sciences to facilitate innovative solutions to global problems. This requires access to high quality biological materials and associated information. It operates on the premise that no one single entity can provide the necessary coverage of organisms and data, therefore the enormous task of maintaining biodiversity must be shared.

Although the goal of the GBRCN was to bring together BRCs from all four domains, animal, plants, human derived material and microorganisms, the demonstration project focus was solely on microbes. Coordination of activities in this domain was well established through activities of national, regional and world culture collection community organisations. The activities of the human derived material community were underway in Europe through the BBMRI - Biobanking and Biomolecular Resources Research Infrastructure but little has been done elsewhere. The animal and plant domains were not represented well in the OECD BRC Task Force and thus were not engaged in the initiative. There was a need expressed by the OECD to demonstrate that the GBRCN would deliver more than current networks and help provide legitimate access to high quality materials and information and thereby facilitate innovation in the life sciences. This was also necessary to convince the other domains of the value of the GBRCN. There was evidence that by coordinating access and adding value to laboratory held, living biological material would enhance legitimate exploitation and improved uptake for global research cross cutting the agricultural, food, healthcare and biotechnological sectors.

The GBRCN Demonstration project Secretariat co-ordinated some activities of candidate microbial domain BRCs (mBRCs) in 15 countries in order to deliver:

- The design for a model network, differentiated from existing organisations
- The Implementation of OECD Best Practice in BRCs (OECD 2007) assessed by independent third parties
- A strategy for the full GBRCN defining its infrastructure and governance mechanisms, its secretariat's structure and scope

Although culture collection organisations have existed for many decades, they or their modern day versions, the Biological Resource Centres have never been fully networked. National, regional and global organisations have endeavoured to help promote collections and have coordinated some efforts. They have brought together metadata on their members to central points and have helped keep members up to date with the progress of science, changing legislation and collaborative opportunities through newsletters, conferences and workshops. However, coordinated strategies for ensuring comprehensive coverage of species and the diversity within them are yet to be put in place. Projects and individual initiatives have made some progress but consolidating the many initiatives that are working towards this goal is crucial to establish a systematic and networked approach. This would bring advantages to both the users and the collections themselves, but importantly provide an infrastructure to underpin research and development, enabling the harnessing of microbial and cell diversity to contribute towards providing solutions to the world's big challenges.

CULTURE COLLECTION FEDERATIONS

The World Federation for Culture Collections (WFCC) has been promoting the activities of culture collections for over 4 decades (http://www.wfcc.info) and has done a tremendous job to help establish a sound operational basis. The WFCC were the first to establish minimum standards for culture collections publishing their guidelines which form the platform on which common operations for networking can be based (Anon 2010). The WFCC, as most culture collection organisations, is a community that exchanges views and ideas. Often this results in the uptake of common approaches but the organisation has no mandate to affect institutional changes in policies and practices. This impedes the introduction of coordinated approaches. At the regional level organisations such as the European Culture Collection's Organisation (ECCO – http://www.eccosite.org) and the Asian Consortium for the Conservation and Sustainable Use of Microbial Resources (ACM - http://www.nbrc.nite.go.jp/e/project01-e.html) work on behalf of collections. They have been very successful in bringing project consortia together to seek project funding to solve common operational problems or address common research issues. There are almost 20 national federations that do similar things at the country level (see Table 1). However, a lot of work still needs to be done both by collections and Governments if the goal to harness the power of microbial diversity is to be realised. We need to harness the properties and products of microorganisms more efficiently if we are to tackle the big global challenges of today in poverty alleviation, food security, healthcare, climate change and the environment. This can be achieved more effectively through networked activities and common infrastructure.

Table 1 National culture collection organisations

Acronym	Network	Link
BCCM™	Belgium Co-ordinated Collections of Microorganisms	http://bccm.belspo.be
SBMCC	Brazil - Sociedade Brasileira de Microbiologia Coleções de	Sociedade Brasileira de Microbiologia Coleções de Culturas : colecao@sbmicrobiologia.org.br Databases : http://www.cria.br

	Culturas	
CCCCM	China Committee for Culture Collections of Microorganisms	http://micronet.im.ac.cn
FCCM	Federation of Czechoslovak Collections of Microorganisms	http://www.natur.cuni.cz/fccm/
CCRB	French Comité Consultatif des Ressources Biologiques	http://www.crbfrance.fr
ECCO	European Culture Collection's Organisation	http://www.eccosite.org
SCCCMOMB	Cuban Culture Collection and other Biological Materials Section;	Contacts: Iglesias: elsie@finlay.edu.cu (President); weng@infomed.sld.cu / ccm@inhem.sld.cu (Vice President); nancy@liorad.quimefa.cu (Secretary); raisi@cecmed.sld.cu (Finances)
KFCC	Korean Federation of Culture Collections	Shinchondong Sodaemunku, Seoul 120-749, Korea
HPACC	UK Health Protection Agency Culture Collections	http://www.hpa.org.uk/business/collections.htm
FORKOMIKRO	Indonesia - Communication Forum for Indonesian Culture Collection Curators	http://www.mabs.jp/kunibetsu/indonesia/indonesia_04.html
JSCC	Japan Society for Culture Collections	http://www.nbrc.nite.go.jp/jscc/aboutjsccc.html
PNCC	Philippines National Culture Collections	Contact: Rosario G. Monsalud, Ph.D., Head, PNCM, rosegm@laguna.net
TNCC	Thailand Network on	http://www.biotec.or.th/tncc/

	Culture Collection	
UKFCC	UK Federation for Culture Collections	http://www.ukfcc.org/
UKNCC	UK National Culture Collection – UK affiliation of national collections	http://www.ukncc.co.uk

The World Federation for Culture Collections (WFCC) was founded in 1963 and is a multidisciplinary commission of the International Union of Biological Sciences (IUBS) and since the separation of the International Union of Microbiological Societies (IUMS) from IUBS in 1979 it has operated as an inter-union commission. It seeks to promote activities that support the interests of culture collections and their users. Member collections of the WFCC register with the World Data Centre for Micro-organisms (WDCM). There are currently over 600 registered collections in 68 countries with almost 5000 staff. 120 of these are affiliated WFCC member collections adhering to the WFCC statutes (http://www.wfcc.info/about/). A congress is held every three years to discuss advances in technology and common policies with regard to biodiversity and the role of culture collections. The WFCC keeps its members informed on matters relevant to collections in its Newsletter and has working programmes addressing patent depositions, biosafety and biosecurity, safeguard of endangered collections, capacity building and quality standards. Since 1986, the WFCC has overseen the activities of the WDCM and it is now the data centre for the WFCC and Microbial Resource Centres (MIRCENs) Network. It was established in 1966 and produced the first hard copy volume of the World Directory of Collections of Cultures of Microorganisms in 1972, whilst based at the University of Queensland, Australia. The WDCM relocated in 1986 to RIKEN, Saitama, Japan and then again in 1999 to the National Institute of Genetics, Japan. It now resides with the Institute of Microbiology, Chinese Academy of Sciences, Beijing, China (http://www.wdcm.org/). The WDCM registered collections hold in excess of 1.7 million strains, 44% are fungi, 43% bacteria, 2% viruses, 1% live cells, and 10% others (including plasmids, plant, animal cells and algae).

The WFCC is the largest independent global organisation that represents professional individuals and culture collections, which preserve biodiversity and enable their proper use. They target living microorganisms, cell lines, viruses and parts and derivatives of them. Key values are authenticity and genetic integrity of the material and validity of the information provided. The WFCC supports the professionals, organisations and individuals with interests in culture collection activities through:

- Networking, providing information and expertise and facilitating communication
- Facilitating access to the collection resources
- Providing training and promoting partnerships
- Encourage the development and implementations of quality and security procedures and the use of common standards and regulations
- Representing member interests in international organisations and fora

- Promoting the establishment of culture collections, their promotion and perpetuation

There are over 120 culture collections affiliated to the WFCC who have agreed to implement the WFCC guidelines (Guidelines for the Establishment and Operation of Culture Collections) and who contribute to the delivery of its objectives. In the growing bio-economy, WFCC's members face increasing global demands for worldwide and controlled access to biological resources, public security, industrial quality of their holdings and associated data and long-term genetic stability of the material. Key to the use of microorganisms from culture collections is the retention of their properties, as research and development must be based on authentic and well-preserved biological material. The WFCC have been helping collections in this respect for over four decades. It is a goal that strains of organisms are supplied from member collections with traceability, conforming to national and international regulatory requirements, and that are preserved in such a way as to retain their full potential.

The European culture collections have collaborated since 1982 when the European Culture Collection Curators Organisation (http://www.eccosite.org) was established to bring the managers of the major public service collections in Europe to discuss common policy, exchange technologies and seek collaborative projects. The organisation opened itself to staff and users of microorganisms and is now named the European Culture Collection Organisation (ECCO). There are currently 66 collections holding approximately 350 000 strains. The members have been involved in producing practical approaches to international rules and regulation. Initiatives led by the Belgian Co-ordinated Collections of Microorganisms (BCCM™) have produced a code of practice for collections to operate within the Budapest Treaty (http://www.wipo.int/treaties/en/registration/budapest/) and the Micro-Organisms, Sustainable Access and use, International Code of Conduct (MOSAICC) which provide guidelines for the operation within the spirit of the Convention on Biological Diversity (http://www.belspo.be/bccm/mosaicc/). There have been several collaborative projects originated through discussions between ECCO members that have placed the European Collections at the cutting edge of culture collection activities and research. The European Biological Resource Centre Network (EBRCN – http://www.ebrcn.net) follows on from the Common Access to Biological Resources and Information (CABRI) electronic catalogue project (http://www.cabri.org).

Most recently EMbaRC (European Consortium of Microbial Resource Centres - http://www.embarc.eu) has continued the output from ECCO member collections. Figure 1 demonstrates the complexity of all the different microbial resource collections, their networks and the project consortia.

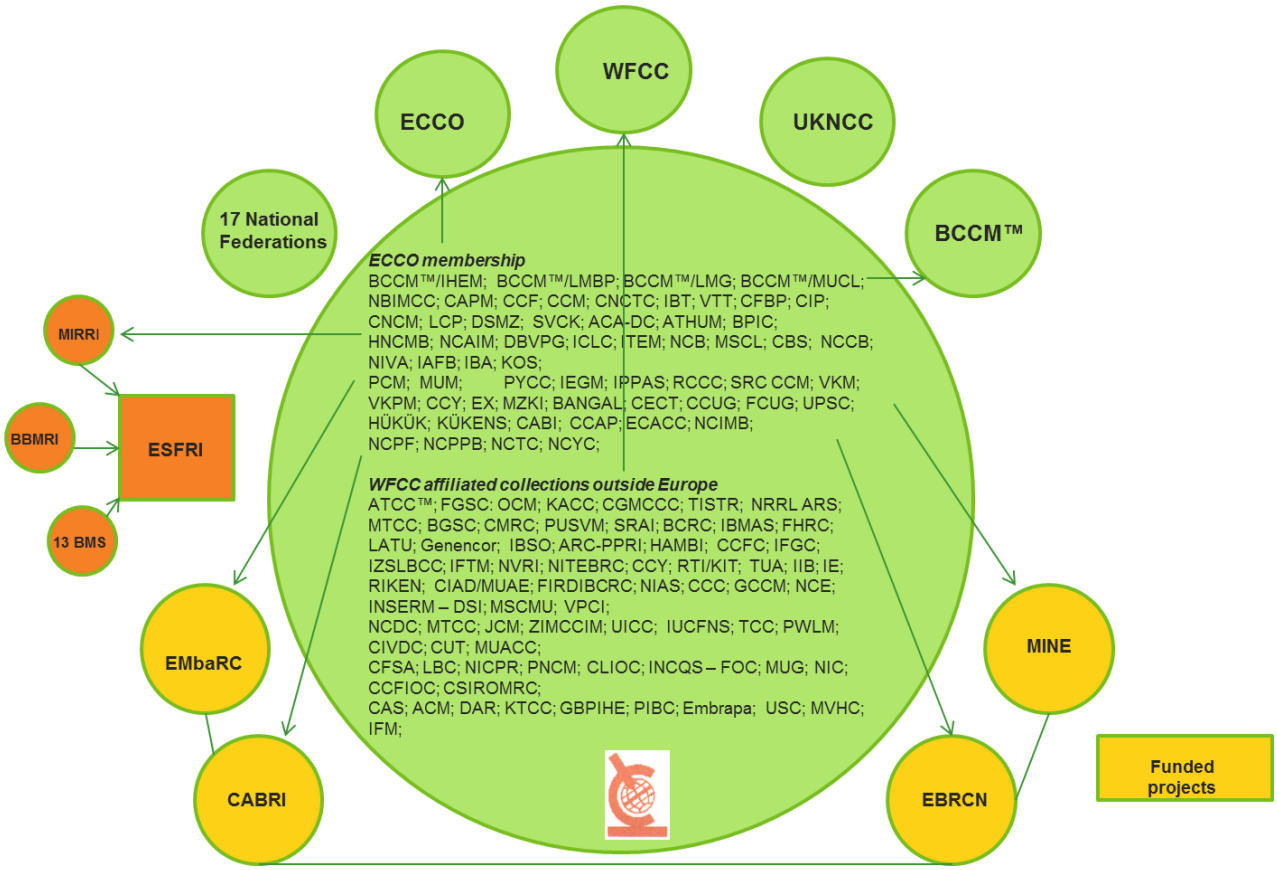

Figure 1 Culture collections: their networks and project outputs present a complicated picture (Acronyms presented in figure 1 are expanded at http://www.wdcm.org/)

The work of the culture collection organisations has been invaluable and has only been limited by their voluntary nature, relying on input of dedicated people as and when they can contribute. Collections need to increase the availability of biological material for the verification of experimental data and the authenticity of reference material used in research. Deplorably, the scientific literature is full of data which cannot be verified because the material is either no longer available and/or the material once used to generate the data has changed or deteriorated. This challenge needs to be met with a coordinated approach requiring an infrastructure to support it. Such strategies cannot be achieved by projects with a defined life span. The GBRCN, ECCO and EMbaRC are bringing together European microbial resource collections with stakeholders (their users, policy makers, potential funders, microbiology societies and the plethora of microbial research efforts) aiming at improving access to enhanced quality microbial resources in an appropriate legal framework, thus underpinning and driving life sciences research. The aim is to provide coherence in the application of quality standards, homogeneity in data storage and management and sharing the workload to help to release the hidden potential of microorganisms. It will be able to focus its expertise and resources to resolve critical problems or towards specific outputs.

RESEARCH INFRASTRUCTURES

The European Strategy Forum for Research Infrastructures (ESFRI) provides the mechanism for the establishment of the Microbial Resources Research Infrastructure (MIRRI); the European node for microbial domain of the GBRCN. ESFRI was established in 2002 to support a coherent and strategy-led approach to policy-making on research infrastructures in Europe, and to facilitate multilateral initiatives leading to the better use and development of research infrastructures, at the EU and international level. ESFRI are establishing pan-European structures to drive innovation to provide the resources, technologies and services as the basic tools necessary to underpin research. The ESFRI strategy aims at overcoming the limits due to fragmentation of individual policies and provides Europe with the most up-to-date Research Infrastructures (RI), responding to the rapidly evolving Science frontiers, advancing also the knowledge-based technologies and their extended use. The microbiology collection community led by the GBRCN Secretariat, ECCO and the EMbaRC consortium have succeeded in placing MIRRI on the ESFRI roadmap. The resultant high quality global platform will be designed to accommodate the future needs of biotechnology and biomedicine. Additionally, the emerging strategy for the EU, Europe 2020 Flagship Initiative, *Innovation Union* calls for coordinated effort and the ESFRI Biological and Medical Sciences Research Infrastructures, that include MIRRI, will help in its realisation.

Innovation has been placed at the heart of the Europe 2020 strategy and is the best means of successfully tackling major societal challenges, such as climate change, energy and resource scarcity, health and ageing, which are becoming more urgent by the day. At a time of public budget constraints, major demographic changes and increasing global competition there remains too much fragmentation and costly duplication. Resources must be spent more efficiently and achieve critical mass. The Innovation Union (EU 2010) sets out an integrated and strategic approach, exploiting and leveraging strengths in new and productive ways. The capacity to create millions of new jobs to replace those lost in the crisis depends on our ability to drive innovation in products, services, business and social processes and models. This demands reforms to get more value for money and tackle fragmentation. EU and national research and innovation systems need to be better linked up with each other and their performance improved. Researchers and innovators must be able to work and cooperate across the EU as easily as within national borders with frameworks for a truly free movement of knowledge. There is a need to get more innovation out of research. Cooperation between the worlds of science and the world of business must be enhanced, obstacles removed and incentives put in place. Europe needs to work better with our international partners. That means opening access to R&D programmes, while ensuring comparable conditions abroad. Establishing a common EU front reducing fragmentation and working together to achieve more effective and efficient advances is what the Innovation Union is all about.

Biological resources, such as microorganisms and their derivatives, are the essential raw material for the advancement of biotechnology, human health and research and development in the Life Sciences. The complexity of legitimate collection, distribution and use of living biological material demands the coordination and sharing of activities. The quality and range of service required by today‘s biotechnology and biomedicine sectors will be delivered more easily through a coordinated network rather than through individual collections. The biological materials held in biological resource centres are employed in fundamental research and find applications in the pharmaceutical area, in agriculture as well as in food industries. It is essential that these materials are not only easily and directly accessible but also that they are of high quality and authentic. The

task of *ex-situ* conservation of biodiversity is enormous and exceeds the technical potential of an individual collection in any individual country. It is a known fact that only a small proportion of microbial diversity is represented in culture collections. Additionally, the number of valid descriptions of e.g. novel bacterial species (which requires deposition of the type strain in a collection) is steeply increasing and this task alone already exceeds the abilities of most collections. The same holds true for other types of biological material as well, e.g. fungi and algae. Adequate collection management of well preserved and authenticated organisms is essential to guarantee quality and safety in the various areas of application, to allow controlled access to potentially hazardous organisms and to ease and improve the use of the materials for health and the environment.

The EU initiative for a knowledge based bio-economy considers the transformation of knowledge from the life sciences into new, sustainable, ecologically efficient and competitive products as an enormous challenge. It expresses the expectation that by 2030 the products of white biotechnology and bioenergy will constitute around a third of industrial production. The information system that will be embedded in the future GBRCN will address this challenge. It will not only provide improved access to biological resources and their related data, but it will allow the combination of related data from other disciplines to produce data landscapes and through modern, interactive tools will allow new interpretations and innovation.

The recent OECD report *The Bioeconomy to 2030: designing a policy agenda* (2009) emphasises that the biological sciences are adding value to a host of products and services, producing what some have labelled the "bioeconomy". The report explains that from a broad economic perspective, the bioeconomy refers to the set of economic activities relating to the invention, development, production and use of biological products and processes. If it continues on course, the bioeconomy could make major socioeconomic contributions in OECD and non-OECD countries. These benefits are expected to improve health outcomes, boost the productivity of agriculture and industrial processes, and enhance environmental sustainability. The bioeconomy's success is not, however, guaranteed: harnessing its potential will require coordinated policy action by governments to reap the benefits of the biotechnology revolution.

THE OUTPUT OF THE GLOBAL BIOLOGICAL RESOURCE CENTRE NETWORK

Thus the key goals of the GBRCN are to:

Support Governments to

- Coordinate legitimate access to high quality resources for research and development helping deliver the national bioeconomy
- Implement international conventions and legislation particularly in biosecurity and the CBD Access and benefit sharing
- Reduction of duplication providing cost effective and efficient cross network approaches

Support Innovation by

- Focussing essential services such as identification of novel organisms, targeting specific chemistry in organisms for further study and protection of public investment made in the isolation of organisms and the generation of information and knowledge by maintaining the link between the biological material and the information
- The honest broker in the conservation and utilisation of genetic resources

What the GBRCN will do

- Networking of networks of BRCs for improved effectiveness and efficiency – giving value for money
- Set and implement coordinated policy and strategies in line with legislation, policy and user needs
- Focus activities to deliver services and resources to meet needs
- Implement best practices in quality management and legitimate operations

What the GBRCN needs

- Engagement in the GBRCN Governance structure
- Financial support for the secretariat activities
- To be consulted as a source of information on policy development in the area of genetic resource conservation and utilisation, biosafety and life science research

The benefits of creating a global network of BRCs was described in the OECD publication on *Biological Resource Centres* the report stresses:

> *International co-operation is needed to provide enhanced worldwide accessibility to information and biological material, co-ordination of standards, linkage between scientific needs and government policies, a framework for regulatory initiatives, a linking mechanism for countries without BRCs and enhanced efficiency reducing redundancies, improve transparency and efficiency and help participants to harness resources.*

Issues that can be delivered better through a research infrastructure over and above what is currently supplied by individual microbial resource collections are:

i. Capacity and strategies to enable a broader coverage of products (organisms)
ii. Facilitate access to limited numbers of microbial specialists
iii. Human resource development programmes to train successors
iv. Bringing together working groups to focus on delivery of resources that meet specific needs
v. Implement common policies that work across international boundaries
vi. Help establish facilities and resources in countries or regions rich in microbial diversity but without resources and facilities to make them readily available for research
vii. Create linkages to data in other systems relevant for data mining and enabling targeting of specific microbial resources for specific tasks – bringing all microbial collection data together creates the critical mass to make this action meaningful
viii. Provide a comprehensive coverage of reference strains
ix. Co-ordinated interaction with other research infrastructures
x. Establishment of a legal operational framework for legitimate and safe access

There is extensive legislation that impacts upon access to, the safe handling, distribution and use of biological resources (Smith and Rhode 2007; Smith 2011, 2012). A number of culture collection organisations exist to help collections keep up to date in a constantly changing legal framework; notably biosecurity, shipping regulations and ethical access and use. Common information resources can be established and common procedures implemented across the network to ensure compliance. Therefore networks can increase single BRC capacity:

- By creating partnerships to access necessary expertise and technology
- By the sharing of tasks to access and utilise the world's biodiversity and creating close links with the user community
- Establishing the virtual infrastructure and encouraging collections to meet the high quality operational standards required today.

The collection and provision of strains presents a challenge for BRCs, the total number of strains isolated, preserved, identified, supplied and utilized each year is not easily estimated. Surveys of the literature carried out by Stackebrandt demonstrate that the deposit of strains that are cited in the literature is dismal. Of 20,200 prokaryotic research strains in 835 articles in eight European journals in 2008, only 190 strains (0.94%) were deposited in public collections (Stackebrandt 2010). These strains are not only needed to facilitate their availability as vouchers for confirmation of results and further work, but deposit is needed to protect the investment made in the research. It is estimated that the American Type Culture Collection (ATCC) supplies around 160 000 individual samples per year (the majority cell lines and not microorganisms), the DSMZ around 20000, but most collections supply a lot less. A more likely figure for those most well used would be 1 to 4 thousand and the majority only a few hundred. Based on this and the fact that there are around 585 collections registered with the World Data Centre for Microorganisms (WDCM) some 0.5 million strains are probably supplied each year. These cover all cell types such as algae, cell cultures, bacteria, fungi, protozoa and viruses. Assuming that over 99% of strains supplied are not from collections, then strains utilized annually is in excess of 50 million. Rather an over estimate, but still a potentially huge number. The concern is that many of the strains provided by non-collections are not authentic and not preserved well, undermining any research done with them. BRCs, operating best practice, need to provide the majority of these strains, rather than the minority, to ensure high quality research is based upon reliable and authentic biological materials.

In 2007 the results of this seven year activity were published, *OECD Best Practice Guidelines for Biological Resource Centres* (OECD 2007). The document delivers the basic rules and best practice as guidance for culture collections. It is intended that BRCs adopt these practices to ensure that users get legitimate and safe access to high quality biological materials and associated information. Implementing a common approach with practices and procedures that allows reproducibility between centres is required. A global network can facilitate implementation of best practices helping individual collections with the process.

BRCs are not just repositories or suppliers of strains. They provide many essential services; of the 585 WDCM registered collections, 85 provide patent deposit services; 295 provide identification services; 250 provide training services; 261 provide various consultation services. There is a diminishing number of microbial taxonomists, bringing together a critical mass is essential to provide a good service. Today where images from microscopes can easily be viewed transmitted around the world the specialist resource of the GBRCN can be accessible to resolve problems on a global basis. Exploration of new environments and ecosystems will be enhanced through access to these specialists enabling problems to be solved and innovative solutions possible. CABI Bioservices performs 2000 identifications per year and similar or higher numbers are performed by other collections; potentially over 0.5 million identifications worldwide; the demand is huge; all research in microbiology must be based on well authenticated specimens. The diminishing

numbers of specialists and increasing use of new automated technologies increases the need for such services. Networking creates a critical mass of specialists enabling training programmes to be developed to pass on knowledge to new specialists and enable comprehensive coverage which individual institutions could not possibly cover.

There is a long way to go before we have access to material representing the 100 000 described species of fungi and the estimated 1.4 million yet to be described. Targeted isolation programmes are needed to make inroads into this enormous task. Additionally, only a small fraction of the described fungal species has been screened for the production of natural products. The use of molecular techniques and high through put screening increases capacity to release fungal potential. Often screening only takes a snap shot of part of an organism's chemistry, expression of genes can be strain specific, indeed genes may have been suppressed in some organisms while others may have multiple copies of genes. Knowledge of the organism's lifecycle, its interaction with its environment, its host or the organisms in its ecosystem are essential to ensure extracts produced for screening access its full potential. The expertise to understand the organism and design appropriate screening strategies is fragmented between institutions but can be coordinated via the network. A network has the potential to coordinate targeted isolation programmes in a legitimate ABS protocol-compliant manner.

Significant effort is being put into ecosystem based approaches where little explored or extreme environments are being studied. The Iwokrama programme was established to demonstrate how tropical forest biodiversity may be conserved and sustainably used for ecological, social and economic benefits (Kelley et al. 2003). 84 of the isolates were found to have potent anti-insect activity, 14 exhibited potent anti-fungal activities and 13 potent anti-bacterial activities. This provided a tremendous hit rate of 1 in 3 although not all will be new active molecules and quite often it is found that activity is due to a combination of molecules in the extract and as a result not easily exploited. The key to the success in this case was:

- Selection of a unique, unexplored ecosystem
- Targeted organisms with unusual properties
- Sampling techniques and analysis carried out by specially trained experts
- Selection of characterisation techniques as de-duplicating tools

The expertise to understand the organism and design appropriate screening strategies is fragmented between institutions but can be coordinated via the network.

The chances of finding active molecules vary enormously, but by ensuring a targeted and structured approach, using appropriate technologies and the employment of the right skills it can be rewarding. In one large programme 13% of the tropical fungi screened for antifungal, antibacterial, antivirals, insecticidal, antihelminthic agents, anti-cancer, diabetes melitus, anti-inflammatory and endocrinological leads using 2 or 4 methods and 2 extracting solvents yielded active compounds (Bills et al. 2001). However, it is not that straight forward as it is estimated there is only a 1 in 250000 chance for an unknown chemical to reach the market. If you have active compounds this increases to between 1: 5000 to 1: 10000 (Crocker 2001; ten Kate and Laird 1999; PhRMA 1998). Chances of active molecule discovery are seen to be enhanced when fungal metabolism can be manipulated (Chang and Todd 2004). Linking this to knowledge of ecosystems, targeted isolation programs can give access to the most promising organisms.

Biotechnology continues to offer a future beyond depletion of our natural resources and can provide a basis for a bioeconomy. More and more natural resource alternatives are being found using whole organisms, cells or cell processes to produce them e.g. biofuels, drugs, neutraceuticals food and beverages. BRCs are knowledge bases necessary to underpin the development of microbiological based industries, which will lead to economic development. Research is underpinned by BRCs, an infrastructure that secures the *ex situ* conservation of biodiversity whist working in a legal and policy framework to enable access and equitable benefit sharing of biological resources. Collections develop isolation programmes, carry out or support organism characterization and screening leading to natural product discovery and added value.

Biotechnology is "a global powerhouse with over $60 billion in revenues and hundreds of marketed products", Pharma makes a $6bn spend on candidate compounds with 12% growth each year and Agbio spends $0.6bn (Szaro 2006). Microorganisms provide an improved route to solutions to several agricultural, environmental, food, forestry and public health problems e.g.: several agents isolated mainly from *Streptomyces* species, are in preclinical or clinical development for the treatment of cancer: Rebeccamycin analog (lymphomas and neuroblastoma.); COL-3 (a tetracycline analog) for advanced solid tumors.; Bizelesin (a CC1065 analog) ; UCN-01 (a staurosporine analog); KRN5500 (a spicamycin analog); 17-AAG (17 Allylamino-17-desmethoxy-geldanamycin) ; FR 901228 (a bicyclic depsipeptide) (Newman and Cragg 2007). Huge revenues from fungal derived drugs remain long after their discovery e.g. cyclosporin, £0.8 billion: and amoxicillin £1 billion. BRCs themselves may not have the capacity to develop all potential organisms into marketable products but through partnerships and coordinated effort can help accelerate the discovery process.

Exploitation of biological materials must be in compliance with conventions, treaties and law for example the Convention on Biological Diversity (CBD). The CBD requires that Prior Informed Consent (PIC) be obtained in the country where organisms are to be collected. Terms, on which any benefits will be shared, must be agreed. The benefits may be monetary but could be information, technology transfer or training. If the organism is passed to a third party it must be under terms agreed by the country of origin. This will entail the use of material transfer agreements between supplier and recipient to ensure benefit sharing with, at least, the country of origin. Access and benefit sharing rules must be followed and signatory countries to the CBD have agreed a voluntary code of practice, the Nagoya ABS Protocol (Anon 2012b). The national implementation of the protocol may well impede access and exchange of materials and information. In this context the collection community will have to work towards a mutually beneficial multilateral operational framework to facilitate science and the discovery process.

Biosecurity impacts heavily on the operations of public service microbial domain Biological Resource Centres (mBRC) hence the activities of the WFCC, GBRCN and EMbaRC. The GBRCN and EMbaRC require the implementation of OECD BRC Best Practice which includes the Biosecurity Guidance as well as aspects of biosafety particularly in regard to implementation of national legislation. Concerns exist on the ability of BRCs/culture collections to implement best practice regarding biosecurity, particularly with the requirement of risk assessment. Another key concern is the lack of easy access to regulations and other information regarding national rules and regulations governing the movement of materials. It is evident that culture collections adopt compliant procedures firstly governed by national laws but specifically compliant with the

Biological and Toxin Weapons Convention (BTWC). They must endeavour to reduce the potential for misuse of biological agents, toxins or associated information or technologies. The Biosecurity Code of Conduct for BRCs sets out an undertaking by mBRCs to tackle their responsibilities and provides a base line for the operation. To this end the GBRCN and EMbaRC projects have designed a Biosecurity Code of Conduct for BRCs which when finalized will be binding for GBRCN members.

A network can focus activities effectively and efficiently through small groups of experts in clusters that can address each of the challenges whether they are BRC or user driven needs. Experience shows with global and regional culture collection organisations such as WFCC, ECCO and national organisations, that a small central body of staff is needed to implement network operation and co-ordinate activities. The size of the central secretariat will be kept small and focussed, much of the work will be done by members working in specialized and focussed clusters for example addressing legal and policy issues, taxonomic groups, focus groups to provide solutions to global challenges leaving the secretariat to manage the day to day operations of the RI with the secretariat reporting to the management board and advised by the scientific advisory board.

Networking has its costs but more than makes up for them in the savings in efficiency and cost effectiveness. The GBRCN is establishing:

- A legal operational framework compliant with international conventions and national requirements to facilitate multilateral activities and agreements and conservation and utilization of genetic materials
- Robust governance structure and Governmental involvement through a Memorandum of Understanding
- Membership agreements that will enable implementation of common practices, procedures and collaborative work programmes
- A user community partnership to ensure the network provides the resources and services required
- Operations using clusters of relevant expertise to deliver efficient solutions and output relevant to the whole network

Essential if BRCs are going to facilitate research, accelerate the discovery process and help address the global challenges of today (Fritze, Martin and Smith 2012).

The GBRCN secretariat would be responsible for:

Managing the technical aspects of BRCs: a quality management system based on international criteria, electronic linkages between BRCs, coordination of catalogues and databases, maintenance and support for BRCs, and development of informatics tools for data analysis, comparison and display

Managing the global network of national BRCs: responsible for administration e.g. membership issues, reporting, budget management, inter-laboratory testing and validation of protocols

Coordinating the BRC initiative with other international initiatives: coordinating the BRC network with existing international frameworks

Providing an intergovernmental forum on BRC issues: facilitating debate organising the forum

Project development and management: proposal writing, seeking funding, project implementation and management

Outreach and publicity: liaising with users to understand their needs; raising the profile of the Network

Organisation and delivery of capacity building programmes: providing programmes, tools, resources and activities

There is a need for funding arrangements for the secretariat which does not undermine or reduce the already tight funding for BRCs. Engagement at the Government level is difficult and more work is needed in this respect. Some countries have preferred the BRCs to contribute with the costs to be met either from additional budget allocation or from existing budgets. History has shown that the collections (BRCs) themselves have no funding for networks and if it costs then they tend not to join. The two main alternatives are therefore:

- Country contributions based upon a country's GDP
- Institutional contributions

There are now over 100 additional candidate BRCs in 28 countries interested in joining the GBRCN. The first new associate member is the Bioresources Collection and Research Center (BCRC) which is part of the Food Industry Research and Development Institute (FIRDI), Hsinchu, Taiwan. There are now over 25 culture collections certified or accredited and the GBRCN could be launched utilising the draft membership agreements and Governance structures that have been designed thus far. However, it would be a BRC run entity and this would not achieve one of the major goals of long-term sustainability. To achieve this essentially means involvement of countries i.e. Governments. The original mechanism considered for their involvement was through a Memorandum of Understanding (MoU) based on the model GBIF use. It would ask countries make commitments for funding the central coordination and provide support for national BRCs. The basic documents and the MoU were published in the third intermediary report to BMBF and the developed tools for establishment of the GBRCN explained in the project final report (Fritze, Martin and Smith 2012). The GBRCN website http://www.gbrcn.org provides much of the information and the additional website on African activities provides specific reports on activities there http://africa.gbrcn.org/. Linking global initiatives to that in Europe with MIRRi provides the foundation stones for the GBRCN. Activities in Asia, where the Asian BRC Network (http://www.abrcn.net/) has become established are paralleled in South America, particular Brazil's contribution to the GBRCN demonstration project. The U.S. National Science Foundation has funded a Research Coordinated Network bringing together USA culture collections in the United States Culture Collection Network (http://www.usccn.org/). The project Atlas of Living Australia (http://www.ala.org.au/) incorporates the data of the culture collections in the Australian Microbial Resources Research Network (AMRiN – http://www.amrin.org) if all are brought together they build the global network (GBRCN). This would provide a firm footing for microbiology research and development.

CONCLUSION

It is essential that the BRC community works together with their users and policy makers to establish a legally compliant operational framework to enable transnational exchange of materials and information. The future of biotechnology and indeed the bioeconomy, depends on the

successful harnessing of biodiversity to deliver solutions to global problems and to accelerate innovation and discovery. Governments, bioindustry and collections must invest to facilitate the release of the full potential of microorganisms. It is evident that mechanisms to fund the developments are needed. This is where the European Strategy Forum for Research Infrastructures (ESFRI) offered us a way forward in MIRRI. MIRRI's preparatory phase, funded by the European Commission, will deliver a suitable operational framework and test it at the global level through the GBRCN.

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