The Pan-European project Microbial Resource Research Infrastructure (MIRRI) has among its goals the elaboration of common policies for BRCs to comply with the Nagoya Protocol on Access and Benefit Sharing of the CBD

Dagmar Fritze and André Oumard, Leibniz-Institut DSMZ-Deutsche Sammlung von Mikroorganismen und Zellkulturen, Inhoffenstraße 7B, 38124 Braunschweig, Germany

Keywords: Microbial Culture collections/BRCs, CBD, ABS, Bio-economy

ABSTRACT

The MIRRI Preparatory Phase project has the intention to build the basis for the construction and operation of a pan-European distributed infrastructure dedicated to microbial resources. MIRRI will support European Research and Development by providing microbiological services, facilitating the deposit of, preservation of and access to high quality samples of viable microorganisms, their derivatives and associated data. MIRRI will establish connections between resource holders, researchers and policy makers to deliver the resources and services more effectively and efficiently, so as to target the needs of innovation in biotechnology and progress in life sciences.

Biological Resource Centres (BRCs) that preserve microbial resources ex-situ and distribute these for science, industrial development and education are key contributors to the Convention of Biological Diversity’s (CBD) main objectives of conservation of global biological diversity and its sustainable use. In that respect, BRCs facilitate the identification of and access to resources, as well as to the associated information in specific public databases. As indicated above, these activities are accompanied by a strong impact of regulations, legislation and policies. This is especially true for the field of Access and Benefit...
Sharing (ABS) and particularly in combination with Intellectual Property Right (IPR) rules. MIRRI’s activities in this area will be to find common approaches for BRCs. These will build upon expertise gained in projects such as MOSAICC\(^1\) and MOSAICS\(^2\) which provided guidance on procedures and documents for issues such as Prior Informed Consent (PIC) and Material Transfer Agreement (MTA), on approaches like the Microbial Research Commons\(^3\) and on practical approaches like the European Culture Collections’ Organisation (ECCO) membership developed Core MTA for the supply of cultures. The design of standard conditions for the deposit/acquisition, maintenance and supply of living microbiological material will be the basis of a confidence-building system to facilitate access and exchange.

A major task of MIRRI will be to establish communication routes to authorities, key players and users and to seek links to and synergies with other domains and initiatives with similar goals on the regional and global level. MIRRI will monitor actions taken by the EU and the member states towards the Nagoya Protocol (NP) and initiate dialogues between microbial resource centres, national and EU CBD representatives, policy makers and other stakeholders to assess practical problems and deficiencies on matters of ABS as well as possible solutions with a view to microbial resources.

**THE GOALS AND IMPLICATIONS OF THE CBD\(^4\) THE POINT OF VIEW OF MICROBIOLOGY AND MICROBIAL SERVICE CULTURE COLLECTIONS**

Articles 1, 8, 9 and 15 of the CBD are of particular relevance to microbiology and microbial culture collections. A condensed version is cited below and the relevant terms or wordings are additionally highlighted. All Articles contain a statement saying that contracting parties agree to support the aims of each Article ‘as far as possible and as appropriate’ allowing room for flexibility depending on national circumstances. Each Article also includes a statement indicating the special needs of developing countries.

Art. 1: …. the objectives of the convention are the conservation of biological diversity, the sustainable use of its components and the fair and equitable sharing of the benefits arising from the utilization of biological resources.

Art. 8(j): …. access to traditional knowledge … associated with genetic resources ….

Art. 9: …. shall complement in situ conservation by establishing and maintaining facilities for ex situ conservation and research on plants, animals and microorganisms; manage ex situ conservation so that resources are not threatened

Art. 15: Contracting parties …. recognise the sovereign rights of states over their natural resources …. shall facilitate access to resources … and not impose restrictions that run counter to the aims of the Convention.

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3 CBD: Convention of Biological Diversity (http://www.cbd.int/convention/text/)
**Access** to natural resources shall be by **mutually agreed terms** and subject to **prior informed consent** …

While Article 15 grants sovereign rights to states over their natural resources, this article does not immediately grant property rights to the state; the question of ownership of genetic resources remains subject to national law.

In the microbiological area and in particular with a view to *ex situ* service collections of microbiological material, this has given rise to varied discussions. Once a culture has been isolated from nature, who of the long chain of value-adding stakeholders might lay claim to it in one or the other way: is it the isolator? or the depositor? any other involved researcher having studied it? the collection(s) authenticating, preserving and maintaining it? the user(s) having received it and performing additional studies? Subcultures of a given organism may be simultaneously in many hands and places. In addition to the natural site where the organism of course persists after a sample had been taken away, it may exist at the same time in several collections worldwide and in several research laboratories. The issue of ‘multiple ownership’ of microbial cultures is being debated. It is the view of most collections that, once a culture has been isolated from nature, no one person or entity can “own” a microbial culture. Rather, the vials containing a microbial culture obtained by a recipient is theirs to use within permissible limits, they may use the contents of the vial subject to certain restrictions. Most collections see themselves as custodians of the strain with a right or “license” to grow the strain, maintain and preserve it for distribution and add data through research.

**THE CBD NAGOYA PROTOCOL ON ACCESS AND BENEFIT SHARING (NP)**\(^5\) **FROM THE POINT OF VIEW OF MICROBIOLOGY AND MICROBIAL SERVICE CULTURE COLLECTIONS**

The NP is intended as an international regime on access to genetic resources and benefit-sharing with the aim of adopting an instrument / instruments to effectively implement the provisions of the Articles of the Convention on Biological Diversity. Below, extracts of some of the Articles are cited which seem to be the most relevant from the point of view of microbiology. In particular Article 2 makes clear that any activity using or handling of biological material is covered by these regulations.

Art 1: … objective of the protocol is the fair and equitable sharing of the benefits arising from the utilisation of genetic resources

Art 2: Definition of Terms:
‘Utilisation of genetic resources’ ….. to **conduct research and development** on the **genetic and/or biochemical composition** of genetic resources, including through the application of biotechnology ..
‘Biotechnology’ …. **any application** that uses **biological systems, living organisms, or derivatives** thereof, to make or modify products or processes for specific use.

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\(^5\) NP: Nagoya Protocol (http://www.cbd.int/abs/text/)
'Derivative' ..... a **naturally occurring biochemical compound** resulting from the genetic expression or metabolism of biological or genetic resources, **even if it does not contain functional units of heredity**

Art. 6: ..... In the development and implementation of its access and benefit-sharing legislation or regulatory requirements, each Party shall **** create conditions to promote and encourage research **** which contributes to the conservation and sustainable use of biological diversity ..... 

Art. 8: ... In instances where the **same genetic resources** are found in-situ within the territory of more than one Party, those Parties shall endeavour to cooperate, as appropriate ....

Art. 16: ..... Each Party shall encourage, as appropriate, the development, update and use of **voluntary codes of conduct, guidelines** and **best practices** and/or standards in relation to access and benefit-sharing ..... 

In principle the NP seeks to cover two main requirements: one is, that signatory countries shall provide a clear national framework of regulations so that legal certainty / predictability of legal decisions is provided to all who intend to access biodiversity in that country. The other is, that signatory countries lay down regulations to the fact that they recognise the legal regulations in other signatory countries set up in connection with the NP. The NP does not require countries to implement restrictions.

In the Annex to the NP examples are listed as to what could be considered as benefits that could be shared between users and providers of genetic resources.
From the length of the two lists (the list for non-monetary benefit is twice as long as the one for monetary benefit) it can be seen that participation in research, institutional and human capacity building is given high priority. This is in particular relevant for microbiology where the greater part of research and development work needs to serve basic science on which then – only in a later step – commercial exploitation could be based which could lead thus to potential monetary benefit.

THE NEED TO SUPPORT AND FACILITATE INTERNATIONAL / GLOBAL COOPERATION

The innovative development of the biotechnology industry and its application to agriculture, health, chemical or energy industries depends upon society’s ability to harness the potential
of biodiversity and what it has to offer: improving health outcomes, boosting productivity of agriculture and industrial processes, and enhancing environmental sustainability.

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. The OECD Report *The Bioeconomy to 2030: designing a policy agenda* (2009)\(^6\) emphasises that the biological sciences are adding value to a multitude of products and services. The expectation is that by 2030 the products of white biotechnology and bioenergy will constitute around a third of the industrial production. Before this background, a growing scientific and economic demand is being witnessed for increasing cooperative research and joint development that is based on living biological material. The necessary consequence out of this demand is a need for increasing global exchange of and access to living biological material. However, exchange and application of living biological material underlies a series of regulations and to enable the necessary access especially on a global scale, coordinated or harmonised processes or in certain cases even standardised processes would be highly supportive.

These would apply for the areas of
- **bio-safety** (import, export, transport; who is entitled to work with which material?)
- **bio-security** (regulated access to material and data)
- **legitimacy** (meeting e.g. the requirements of CBD)
- **quality** of material and data (comparability under QM aspects)

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• **stability, purity, authenticity, performance** of the material (comparability under scientific and systematic aspects)

Such coordinated processes would in turn favourably enhance accessibility of material and data and boost innovations and development.

Unfortunately, a counterproductive development seems to happen in connection with countries implementing nationally the NP. In some of such approaches it seems to be tried to prepare ‘watertight’ ‘all inclusive’ national regulations, and researchers report that these regulations rather strangle research efforts, than support it. So far, ABS relevant legislation seems to be unclear in most countries or does not yet exist. Where it seems to exist, competencies and procedures are often not clear. Reportedly, it is often difficult to find out which authority to address for which question and for which permit; or which permit would be needed for which action and in which sequence. Even among themselves, authorities often seem to be uncertain about this, which results in extremely difficult situations for researchers. Recently, it has been communicated that e.g. Brazil, who were among the first to set up a comprehensive national ABS framework, have revisited their legislations and put in place facilitated regulations. Their own researchers had been too heavily and negatively impacted by their regulative framework, so that a revision was felt necessary. It has been reported that one main change concerns the high originally up-front administrative work that has now been shifted as much and as far as possible towards the end of the whole process to a point where a potential benefit might become visible.

A danger that emerges through establishing too high hurdles, is the fragmentation of research and ceasing of cooperation because researchers cannot afford to ‘waste their time’ with unnecessary bureaucratic paper work. Voices of researchers in microbiology are indeed heard saying that they would then rather go sampling and isolating new organisms from their own local environments and study them in isolation, than to have to face months of paper work distracting them from research. A scientifically and socially unacceptable consequence could be the duplication or multiplication of the same research being done in parallel by several scientists in the world, not knowing from each other’s work. Individual countries’ development would be hampered, resp. their researchers left alone and behind from scientific progress. Research money would be wasted and knowledge lost. Similarly, it would have to be expected that deposit of genetic resources in service collections for open access would cease and in consequence biotechnological developments and applications would be severely impaired.

**WHY DOES MICROBIOLOGY NEED A DIFFERENT / FACILITATED APPROACH?**

In many Articles of the NP differentiation is made between providers and users of genetic resources. However, with respect to microbial resources it has to be considered that the differentiation into providers and users of microbial genetic resources is not clear cut; all countries or regions can be providers and users at the same time. In particular, microbial collections do not operate as ‘users’. They are rather brokers between providers (who could be all countries, individual researchers as isolators, descriptors and depositors of microbial
diversity) and users (again these could be all countries or individual researchers in research and development as recipients of microbial diversity).

In contrast to botany and zoology only less than 0.1% of all microbial diversity is known today. Thus most of the research done in microbiology must serve basic science: increasing knowledge, inventoring, understanding complex ecosystems, revealing metabolic and katabolic abilities, etc. Any ecosystem still harbours a plethora of yet unknown microorganisms.

Microorganisms are not geographically confined. They are easily transported across boundaries by wind, water, dust and animals. Humans carry them on their skin, shoes and clothes. Photographs taken from satellites e.g. reveal the large dust clouds that cross continents and oceans in case of storms which carry myriads of microorganisms with those dust particles.

Photographs taken from [http://www.spiegel.de/wissenschaft/natur](http://www.spiegel.de/wissenschaft/natur); origin NASA. See on each picture on the left the coast line of South America, on the right side the West African coast line and the dust clouds crossing the Atlantic Ocean.

Hence microbial diversity can only be exploited for the benefit of mankind through cooperative international / global research efforts.

In this context, the issue of commercial versus non-commercial use of microbiological material would need further definition. Any result out of basic microbiological research can one day be picked up and used for commercial use. A recent suggestion was made to use e.g. the fact of publication or non-publication of research results as a means for differentiation.
WHY DO RESEARCHERS DEPOSIT THEIR STRAINS WITH A MICROBIAL SERVICE CULTURE COLLECTION - FOUR MAIN REASONS TO DEPOSIT

The deposit of Type Strains
Following the Concept of Valid Description of Species and Validation of Names (International Code of Nomenclature of Bacteria) which lays down rules for the description of a bacterial species it is required to designate and deposit the type strain of the species and to publish the new name in the International Journal of Systematic and Evolutionary Microbiology (IJSEM, previously IJSB) or in its Validation Lists.

Most important in this context is Rule 30 which demands: '.. a viable culture of the type strain of a given species must be deposited with two public service culture collections, located in two different countries, from which subcultures would be readily available.'
Yearly more than 700 new species are described in bacteriology and their type strains deposited.

The deposit of strains for patent purposes according to the Budapest Treaty
To be able to rework especially biotechnological inventions which involve living biological material, it might be required by patent law to deposit this biological material in a recognized International Depositary Authority (IDA), so that this material becomes available to authorized third parties without undue restrictions. Most of the larger microbial service collections have acquired the status of IDA vis-à-vis the World Intellectual Property Organisation (WIPO). The Budapest Treaty regulates in detail the obligations and rights of patent offices, patent holders, depositaries and third parties with respect to the microbiological material and related data.

Scientifically interesting microorganisms and Biotechnologically / biomedically interesting microorganisms
For researchers who study and publish scientifically interesting features of microorganisms, e.g. metabolic pathways, life in extreme environments, micro-ecosystems, end products, degradation abilities, etc. it is in most cases not mandatory to deposit. The same is true for researchers who study and publish new features of particular microorganisms for biotechnological or biomedical applications, such as e.g. enzymes for degrading substances, for converting and building up substances, or other compounds such as dextrans or glycosides. However, both types of deposit are made regularly on the free decision of researchers, triggered by their own interest or the interest of their institutions to contribute to the furthering of research in life sciences. In addition, today more and more scientific journals encourage authors to deposit the biological material under study in service culture collections for safeguarding continuity in scientific progress. Whoever does research and publishes is using previously published information and know-how and thus should accept an own responsibility as a link in the knowledge chain.
Data can only be verified if the biological material they pertain to is available for comparison and further study. Furthering of research can only be done if new research can be built upon existing results and the related tools: trustworthy data and authentic biological material. This is also the main reason why researchers work with organisms obtained from *ex situ* service culture collections. Without this supportive service, scientists would constantly have to conduct the skilled and expensive processes of isolation, characterization and identification of organisms at the start of each new study.

To demonstrate the extent of exchange of microbial living material worldwide and the measures taken voluntarily by microbial resource centres, a few figures and facts are given below on the deposit and supply of living microbiological material using the example of the DSMZ.

The DSMZ stock of cultures amounted in 2011 to ca. 23,000 cultures listed in the open catalogue. Additionally ca. 8,800 cultures had been deposited for patent purposes. On average, DSMZ receives for deposit annually ca. 1,000 strains (as a service collection DSMZ receives these cultures usually without requesting them). These cultures come from researchers all over the world, on average from ca. 70 different countries. On the other hand, DSMZ supplies annually ca. 21,000 samples of living microbiological materials to authorised third parties. About half of these cultures go to researchers and institutions worldwide in ca. 70 countries. Overall, in the World Federation for Culture Collections (WFCC), supply and exchange of microbiological material amount to more than 500,000 samples annually. Imagine the amount of work that would pile up, if for each and every action bilateral agreements would have to be worked out.

DSMZ has, like all major service culture collections given themselves standard procedures and processes serving the aims of CBD ABS of transparency and traceability, which are

- registration with the World Data Centre for Microorganisms (WDCM)
- request for information on country of origin on accession form (since 1993 no acceptance without this information)
• request for information on PIC on accession form
• assignation of an individual accession number to each biological material
• individual data entries for each biological material, showing the complete history that is available for this material
• catalogues of holdings are published and regularly updated
• information on the CBD and the resulting responsibilities for depositors and recipients is provided
• implementation of the ECCO agreed Core MTA for the supply (‘no passing on to third parties’; ‘if commercial use – contact country of origin’)

MIRRI – THE PAN-EUROPEAN MICROBIAL RESOURCE RESEARCH INFRASTRUCTURE\(^7\)

The origin of MIRRI lies in the European Strategy Forum for Research Infrastructures ESFRI which had been set up in 2002 by the Competitiveness Council. This Forum is independent from the European Commission and is composed of the Member States and representatives of the European Commission. In recognition that good and innovative research needs to be supported and underpinned by appropriate high quality infrastructures, this body’s goal is to describe the scientific infrastructural needs of Europe for the next 10 to 20 years and to identify vital new European Research Infrastructures of different size and scope. In 2004 the Forum received the mandate from the Competitiveness Council to develop a European Strategic Roadmap for Research Infrastructures.

\(^7\) MIRRI: Microbial Resource Research Infrastructure (http://www.mirri.org/)
The map shows countries in which a MIRRI partner, a collaborating party or an ECCO member collection is located.

The MIRRI project idea had, after submission, immediately been recognised by the ESFRI Council and added to the Strategic Road Map in 2010. A subsequent project proposal to the EC was successful and MIRRI will start its work at the end of 2012. The MIRRI project will provide microbiological services facilitating access to high quality microorganisms, their derivatives and associated data for research, development and application. It will connect resource holders with researchers and policy makers to deliver the resources and services more effectively and efficiently to meet the needs of innovation in biotechnology. It will add value to the microbial resources and services needed for research and thus accelerate the discovery process. To make this possible in a coordinated and comparable way the partners will implement the OECD Best Practice for microbial BRCs.

In the Preparatory Phase (2012 – 2015), the focus of the project will be on governance and structure, as well as on technical, legal entity and financial issues. In that phase the links within the RI - the microbiological resource centre community - and between the RI and its user communities, policy makers and potential funders will be established. The Preparatory Phase will lay the foundation for the next step: to enter the Construction Phase for the infrastructure which is expected to run for another three years.

MIRRI is an integrative initiative that brings together a critical mass of loose networks, projects and initiatives to provide a solid structure that can act as a distributed but coordinated service provider. It will build upon the achievements reached by the European Culture Collections’ Organisation (ECCO) and national networks of microbial culture collections and on regional initiatives such as the European Consortium of Microbial Resources Centres (EMbaRC) and the Common Access to Biological Resources and Information (CABRI). It firmly takes into consideration global initiatives such as the OECD
BRC Initiative and its Best Practice Guidelines\(^8\) and the Global Biological Resource Centre Network Demonstration Project GBRCN\(^9\) emanating from an OECD Working Party on Biotechnology initiative and having been supported by the German Ministry of Education and Research.

Examples of services to be provided are, e.g.:
- Supply of authentic control and reference strains, incl. DNA and RNA
- Identification of microorganisms by state of the art technologies
- Strain typing and authentication
- Characterization of isolates
- Screening, providing lead natural products
- A range of testing and consultancy services at accredited facilities
- Assistance in management of invasive species
- Improved production in crops and commodities
- Storage of strains for public access, safe, private and patent deposit
- Detection, enumeration and isolation of microorganisms
- Material resistance testing and bioassays
- Detection and quantification of microbial toxins
- Secondary metabolite profiling, bio-control
- Mycoplasma elimination from cell cultures

With a view to CBD and ABS issues, MIRRI will take into consideration previous activities of the culture collection community for a binding framework for BRCs. Among these are, e.g. the WFCC database system *World Data Centre for Microorganisms*. Members are registered through a unique acronym and numerical identifier and are urged to catalogue their microbiological resources allowing tracking of microbiological items. The MOSAICC project *Micro-organism Sustainable Use and Access Regulation International Code of Conduct* (http://www.belspo.be/bccm/mosaicc) had dealt with ABS issues on Material Transfer Agreements and Prior Informed Consent. This has resulted in an ECCO agreed Core MTA for the Supply of Cultures (www.eccosite.org).


MIRRI's goals are to support developments towards a favourable environment for research and application in the European Area. This in mind, the partners to MIRRI together with renowned experts in the field will tackle coordinated approaches to ABS in microbiology and participate in respective regulatory discussions. A chance would be seen, e.g. in the harmonisation of national legislation under an EU wide framework. Additionally, EU cooperation with other non-EU regions / countries with respect to standardisation and harmonisation of regulations would greatly support joint research.

\(^8\) Best Practice Guidelines (http://www.oecd.org/science/biotechnologypolicies/38777417.pdf);
\(^9\) GBRCN: Global Biological Resource Centre Network (http://www.gbrcn.org/)
Potential schemas for approach to ABS should take into consideration the main three steps in working with microbial biodiversity (1) collecting samples *in situ* and isolating organisms from collected material (2) deposit of organisms in *ex situ* collection where the organism is subcultured, purified, authenticated, characterised, preserved, catalogued and supplied (3) use of the organism in research and development. These three steps might be regulated individually and differently, while for step two it should be tried to develop an overarching agreement to clearly describe the rights and duties of service culture collections / BRCs and thus making one-to-one agreements unnecessary.

**SUMMARY**
The CBD-ABS regulations will be implemented on individual national levels. As a consequence (and examples already exist), a multitude of national legislations and national competent authorities are to be expected; a multitude that might adversely impact on research and development. Being strongly shaped from and for zoological/botanical issues, the expected regulations might (unnecessary!) adversely impact on science and development especially in microbiology and on microbial *ex situ* collections. It has to be reiterated that ‘user’ and provider’ cannot be differentiated easily in microbiology. Essentially, any researcher from any country, who is going to collect e.g. soil samples in his own or another country, and will be isolating microorganisms and doing research on them, is a ‘user’. However, huge up-front costs might emerge on all sides, without knowing whether any economic success can be expected to pay for it. To avoid negative impacts as far as possible, common approaches to compliance are needed wherever possible as well as education of governing bodies, academia and industry. Tailored solutions should be designed for microbial collections / BRCs who are tools promoted by CBD Art. 9 and who have a special role in the process that ensures resources are available for the enhancement of science. There is a clear demand for the networking approach delivered by regional, interregional and global collaboration.