Executive Summary:
Microbial organisms, such as Archaea, Bacteria, yeast, filamentous fungi, and the component parts thereof, e.g. phages, plasmids and DNA, as well as data associated and analytical tools are the central key material for the advancement of research in basic and applied studies in academia and the bioindustry. Microbial samples are used in a wide spectrum of basic and applied research, ranging from high-throughput techniques at the genetic and epigenetic level to improved food, health and the environment. The importance of microorganisms as the essential raw material for the advancement of biotechnology, human health and research and development in life sciences has been recognized by the OECD and the term microbial domain Biological Resource Centres (mBRCs) coined for public culture collections run under an approved quality management. It was the long successful interactions of major European mBRCs that provided the grounds to move the mBRC interactions to a higher interoperative and harmonization level. The European Commission (EC) has granted 3.1 Mio € funding (2012-2015) to the Preparatory Phase of MIRRI (www.mirri.org) to conceptualise and secure funding for the construction of the European Microbial Resource Research Infrastructure. During the Preparatory Phase MIRRI was managed by the Leibniz Institute DSMZ - German Collection of Microorganisms and Cell Cultures GmbH, Braunschweig (Germany). At the beginning of the project the MIRRI consortium embraced 16 partners from 11 countries and 17 Collaborating Parties. As the latter number increased to 28 today MIRRI constitutes a network that now encompasses 19 European countries.

The objectives addressed by the MIRRI consortium during the Preparatory Phase were to develop strategies to integrate existing quality controlled public microbial resource centers and public microbial culture collections into a pan-European microbial resource research infrastructure under a legal status, replacing the fragmented landscape of holdings, data and services by a coordinated offer to the academic and bio-industrial user to foster research and the bio-economy. MIRRI achieved most of these objectives by not only creating an operational concept for a sustainable infrastructure, developing policies for harmonized accession, data management, compliance with the main objectives of the Convention on Biological Diversity and on biorisk assessment and biosecurity measures but also to provide the grounds for the creation of a knowledge base platform. A specific challenge is the generation of an IT-infrastructure capable
of linking microbial resources with the wildly dispersed genetic, molecular and phenotypic data stored within mBRCs, public databases and the literature.

At the end of the Preparatory Phase MIRRI has not yet achieved the commitment of countries to proceed with the application of a legal status. Though encouraged by the mid-term review assessment and national stakeholders’ approval of achieved goals, MIRRI will advance into the Transition Phase without funding and without the indication of the statutory seat. Individual MIRRI partners will participate in H2020 projects, i.e. EMBRIC and CORBEL, and as MIRRRI will stay on the ESFRI roadmap until 2020 it will continue to apply for national and international funds. The main goal, however, will be the continued pursuit to convincing nations to invest in MIRRI.

Project Context and Objectives:
The project content and the action plan of the Preparatory Phase of MIRRI (MIRRI-PP) were defined in the Grant Agreement with the EC. The 10 Workpackages (WP) of MIRRI encompassed the specific deliverables aimed at integrating major European quality-controlled public microbial domain Biological Resource Centres (mBRCs) together with their supportive technologies into a novel pan-European resource research infrastructure.

The operational concept of MIRRI (Business Case) for the next stage has been developed based on the experience gained during the Preparatory Phase. From the beginning it was decided that the national nature of mBRCs with their associate databases required a distributed structure for MIRRI. The hub (Central Coordinating Unit, CCU) and spoke (national mBRC or network of national mBRCs, National Node) structure adopted has been the basis for harmonizing (1) accession policies, (2) ensuring provision of high quality resources, services, training and expertise, (3) compliance with national, European and international laws, and (4) actively supporting applicable cluster activities to foster knowledge sharing, innovation and development arising from interactions with users and providers of MIRRI. The ultimate goal was outlined to provide a central knowledge-based platform to link all aforementioned activities through expert clusters for collaboration between academia and industry and to foster training and education.

The key objectives during the Preparatory Phase of MIRRI were:

1. Management of the MIRRI project and design of the governance and legal structure to provide the scientific, technical, ethical and legal basis for the construction and operation of MIRRI;
2. Analysis of user and stakeholder needs and expectations for developing appropriate communication channels;
3. Development of criteria for MIRRI partner membership and user access;
4. Gap analysis of MIRRI partner holdings, services, instrumentation and tools;
5. Realization of schemes of future dissemination activities: training courses, university curriculum for Master and PhD students;
6. Exploration of evaluation criteria to measure the impact of MIRRI on society and of the user clientele on MIRRI;
7. Outlining a strategy for data standards for strain acquisition and interoperability of datasets from various sources to maximise user attraction to MIRRI;
8. Defining the position of MIRRI partners in the legal framework of resource property rights and ownership.

Microorganisms such as Archaea, Bacteria, yeasts, filamentous fungi, phages, and the component parts thereof such as plasmids and DNA as well as data associated to those and analytical tools are the central key material for the advancement of research in basic and applied studies in academia and bioindustry. Microorganisms have been used for more than 150 years for deciphering the agents of human infections and they serve as natural resources for the production of antibiotics and other secondary metabolites of therapeutic value; they play fundamental roles in the cycling of gases, and they are key players in improving food, agriculture and waste management; they are appreciated tools in studying the evolution of early life on planet Earth, of phylogeny, ecology, physiology; they are key research tools for determining changes in the genome, transcriptome, proteome, or metabolome for unravelling genetic and environmental factors determining the mechanisms of their beneficial and detrimental actions. Consequently, microbial resources are considered as essential raw material for the advancement of biotechnology, human health and research and development in life sciences and researchers have relied upon the availability of reference material from microbial culture collections for more than 120 years. Europe has been the cradle of public collections and their presence in the respective national research environment is an indispensable element for the advancement of science. At the European level, however, the landscape is fragmented, lacking coherence and coordination. This is the situation the Microbial Resource Research Infrastructure (MIRRI) will resolve; it will integrate the main microbial resource centres and their supporting services and data into a novel pan-European coordinated microbial Research Infrastructure. This will result in the establishment of a higher level quality-controlled entity, strengthen the science base, improve cross-border coordination and develop standards. All of these are important contributions to respond to the grand societal challenges, i.e. understanding ecology to improve the quality of the environment (climate change), health and food safety.

The density of European high-quality mBRCs, their combined offer of resources, technical and expertise and services is unparalleled in the world. If mBRCs receive adequate support and are able to solve the technical issues and maintain societal acceptance, a pan-
European Microbial Resource Research Infrastructure (MIRRI established as a legal entity, e.g. MIRRI-ERIC) will become a major participant in addressing all those grand challenges which require solutions from microorganisms. On the one hand, the offer, expertise and service of mBRCs often stand in strong contrast to the attitude of scientists from academia and the bioindustry who do not take full advantage of this superior source. As demonstrated for bacteria about 70% of the reference strains used by authors in scientific studies as reference strains were obtained from peers and laboratory collections, thus of potentially doubtful authenticity. On the other hand, less than 1% of bacterial strains used in scientific communications were deposited in public collections (Stackebrandt, 2010). It is evident that the biological materials on which published data has been generated must be available to check when aberrant or erroneous results are discovered or when new technologies are available for further study and characterization. The offer of major European public service collections, combined in the MIRRI project, to accept resources during or shortly after publication is a spark to ignite the participation of other such collections worldwide. The rationale for doing so is not based on a concern that authors are incapable of short-term handling of research strains; it is based on the fact that microbial resource centres have decades of experience in handling, safeguarding and shipping a wide range of diverse material that is otherwise prone to involuntary loss by negligence or deliberate clearing of laboratory holdings. The public service collections/mBRCs comply with applicable regulatory requirements, provide material under material transfer agreements settling terms and conditions of supply and governing intellectual property in relation to international conventions, protocols and treaties. mBRCs as service collections are equipped with high expertise and technical requirements in a wide spectrum of general and applied areas which are often missing in the academic environment. Here, mBRCs can play a decisive role in complementing academic curricula by broadening the range of topics otherwise not offered by universities. It is especially the integrated analysis of complex microbial interactions, ranging from the isolation of a specimen from the environment to the description of novel species, deciphering the genomic information and its path to gene expression. Targeted identification of genes of interest for biotechnological exploitation as well as analysis of ‘microbiomes’ make mBRCs interesting partners for industry and ‘personalized medicine’, respectively. All this requires efficient collaboration between mBRCs and users from academia and industry.

This was the scientific background where this project of 16 partners and 17, in the end, 28 Collaborating Parties from 19 European countries joined MIRRI under a defined quality level and prepared to finalize its Preparatory Phase. The WP structure of MIRRI clearly demonstrates that the work has helped to find solutions and outline strategies for many of the different key issues. The success is further demonstrated by the fact that certain elements of national mandates such as those indicated in the Partner Charter (see http://www.mirri.org/legaldocuments.html) were subordinated for the greater good, e.g. a harmonized accession policy to broaden the depth and breadth of microbial resources, the creation of collection ‘light houses’ to avoid redundancies in holdings and the identification of centres of expertise. For improved communication MIRRI has developed a concept for a knowledge-based platform, on which all currently disparate individual offers will be managed and made visible and accessible through a single access entry point, guiding the user to different MIRRI offers, such as Expert Clusters, training and education, services and access to technology, knowledge and facilities. The underlying “Collaborative Work Environment” (CWE), is projected to be established in the MIRRI Transition Phase. The ultimate goal of a functional platform includes access and cross-interoperability to all of its areas, no matter from which individual point of interest a user approaches.

The outlined strategies, governance and proposed financial plan of the MIRRI-PP has been outlined in the 51-page draft 3rd Iteration Business Case (IBC) which has been sent to all national governmental stakeholders and discussed in the course of two stakeholder meetings. The IBC summarizes the added value of a coordinated infrastructure of mBRCs as compared to the action and business of individual mBRCs which alone cannot present solutions to global microbial needs. No single national mBRC or a network of mBRCs offers a complete coverage of microbial diversity and associated services. By working together MIRRI makes the best of present capacities, bridges gaps and addresses the needs of biotechnology and academia today, such as:

- Offering an integrated spectrum of equipment, data, background knowledge and services to explore biodiversity;
- Substantial increase in provision of type-reference- and voucher strains to the entire spectrum of users via a single ‘entry’ point;
- Setting European standards of collection, curation and analysis;
- Sharing best practices, standards and personnel by staff exchange, curricula and course organisation for continuing professional development.

Another major achievement laid down in the IBC is the envisaged role of MIRRI in driving a successful bioeconomy. Four elements are built on one another to form a cycle of an inter-related whole. These elements will include protection of investment by safeguarding valuable resources, coordination of offer and expertise, a holistic approach to data management and an integrated solution. Based on a series of questionnaires an inventory of taxonomic hierarchy-based resource holdings, methods used for resource authentication, services, teaching and education has been carried out for partner mBRCs which formed the basis for the beginning of discussions among heads of mBRCs to initiate a harmonization process. These meetings formed important milestones in the history of European mBRCs which, until the emergence of MIRRI, followed national mandates rather than looking at an integrated solution to
streamline individual business and developing an improved offer to national and international users. A technical advantage of the MIRRI-PP was the feasibility study of major databases housed in three different mBRCs [www.bacdive.dsmz.de www.straininfo.net www.bioinformatics.hsamartino.it:8080 (USMI Galaxy)]. This comparative approach led to the recognition of limitations in content, differences in user interfaces, lack of inter-connections and heterogeneity in data models and formats. It also provided solutions for a harmonized approach such as providing mBRC catalogues in a common format, validation of catalogue contents, interconnectivity of domain information systems for data extension, provision of a unique portal for catalogues and associated data as well as design of an interoperable system based on application programming and service based interfaces. Technical solutions for an interoperable system has been moved to the MIRRI Transition Phase as novel funding sources are needed.

A further advancement was the analysis of stakeholders in which the main types of stakeholders of potential interest in MIRRI were identified, and their level of engagement and the goal of interaction, from the viewpoint of MIRRI partners, defined. The categorization of stakeholders based on their power over, and their interest in MIRRI, resulted in the definition of four groups, termed Allies (the majority of stakeholders though with varying degree of both criteria), Supporters, Latents and Bystanders. This analysis will allow a targeted approach to promote and lobby MIRRI interests.

The governance structure of MIRRI will consist of a not-for profit network using the hub and spoke topology to connect the different national mBRCs or mBRC networks via National Nodes (NN), with the Central Coordinating Unit (CCU). Services, resources and data are channelled through National Nodes to the CCU platform, while heads of mBRCs and National Node coordinators advise and implement the joint coordinated activities at the national and institutional levels. The CCU is a central element of the MIRRI governance structure providing the administration and support services for the general management and administration of the envisaged legal MIRRI entity; it is the central point for communication with stakeholders and is responsible for the promotion of the infrastructure. The CCU is connected to the NN bringing together the national partners (mBRCs, experts and service providers) that meet the MIRRI requirements. Access to the MIRRI offer will be via a virtual portal, directly via mBRCs or their NNs. All these functions require funding through revenue lines and Member State funding mechanisms. The MIRRI Financial Plan addresses not only the central costs of the MIRRI outputs but also the costs associated with the running of the NNs and capacity building in the national mBRCs themselves to meet the Partner Charter, the requirements to deliver MIRRI’s objectives. Based upon the Financial Plan, the German Ministry of Science and Technology (BMBF) required an adjustment of state contribution, requesting at least 90% self-sustainability of MIRRI after 5 years of operation.

Income streams were subsequently identified and a new Finance Plan provided to national governmental stakeholders. A Contingency Plan evaluated the risks and presented a spectrum of risk mitigation actions.

The strategic work of MIRRI-PP had several dimensions and can be looked upon from different perspectives. MIRRI has developed a legal operational framework by which it can assure compliance of its partner mBRCs with the Nagoya Protocol on Access to Genetic Resources and the fair and equitable Sharing of Benefits (ABS) arising from their Utilization to the Convention on Biological Diversity (CBD). MIRRI has an agreed Policy statement on how MIRRI partner mBRCs commit themselves to contributing to reaching the main objectives of the CBD while operating in compliance with all applicable national and international laws on ABS and regulatory requirements.

MIRRI will be responsible for the provision of the highest possible quality of resources and data to support research excellence. It will add associated data from in-house research to public databases to enlarge the knowledge base. The infrastructure will help to create national networks of mBRCs to facilitate communication, avoid redundancies and harmonize the IT structures.

MIRRI will bring cohesion to the hitherto fragmented landscape of European mBRCs by forming an infrastructure on the foundation level with similar initiatives progressing in East Asia and South America. Speaking with one voice, MIRRI has substantially more weight than individual mBRCs in developing trust among the global landscape of microbial infrastructures. The common basis of the ABS regulation will facilitate access to foreign microbial resources from countries with mega-diversity with benefits for the European bio-industry.

The main weakness of the PP scheme in MIRRI perspective was overly optimistic estimation (originally three years) of the timeline needed to engage and commit Members States to the Construction Phase.

The main bottlenecks identified in the transition from MIRRI-PP to the Implementation Phase (legal MIRRI entity) are:
(1) Only five countries signed a Memorandum of Understanding (France, Greece, Latvia, Poland, Spain). The national representatives of these countries as well as those from Belgium, The Netherlands, and Italy advised MIRRI to delay subsequent stakeholder meetings until at least four additional countries, including Germany, had signed the MoU. Subsequently, further discussions on legal structure, budget, governance structure and voting rights were not made.
(2) Member mBRC representatives find it difficult to identify the most appropriate national stakeholder that will represent National interest in MIRRI. Individual national mBRCs are under the legal custody and finance schemes of quite different authorities and each mBRC had to find its way through complex hierarchic structures of ministries.
(3) Despite the initial breakthrough in getting mBRC managers to discuss strategy together and collaborating for more than 50 years many mBRC heads are still reluctant to openly commit themselves to certain MIRRI goals, especially to a harmonized accession policy. Though they agree to the MIRRI Partner Charter, they still retreat to national or even institutional mandates and the sometimes the long
With the end of the MIRRI-PP the financial support for MIRRI will cease. However, the work will continue and the above issues will be addressed as far as possible. Individual partners of MIRRI are members in H2020 projects such as EMBRIC (www.embric.eu) Rittrain (www.ritrain.eu) and CORBEL (www.corbel-project.eu). MIRRI will stay on the ESFRI roadmap until 2020 and partners will continue to apply for H2020 grants. The host of the MIRRI secretariat DSMZ will support a small coordination bureau to stay connected with partners and several partners are committed to continue both the central activities and continued effort to engage nationally. The MIRRI website (www.mirri.org) will remain active providing information on developments.

Project Results:
The following section presents a summary of the main results and progress towards objectives of the Work Packages (2-9) during the operation of the MIRRI-PP. More detailed descriptions of the deliverables is available in the Deliverable reports.

For more than a century microbial resources have been recognized as the essential raw material for the advancement of health, and later for biotechnology, agriculture, food technology and for research in the Life Sciences. It was soon recognized that maintaining and providing live cultures to foster and support the development of basic and applied science was essential. This led to the establishment of microbial culture collections in various European countries. In addition to large and comprehensive public not-for-profit national collections (microbial domain Biological Resource Centres, mBRCs) a wide range of non-public academic and industrial collections (Culture Collections, CC) were founded, embracing a narrower spectrum of taxonomic diversity of research and application interest. Only in a few countries did mBRCs and CCs form networks to streamline basic procedures of acquisition and provision. mBRCs and most of the larger CCs are members of the World Federation for Culture Collections (WFCC) and the European Culture Collections’ Organization (ECCO), both of which are mainly interest groups rather than entities with decisional power. In Europe several mBRCs, often from different countries, share four decades of collaboration, partly on common research interests, partly on harmonizing managerial, data and best practise issues (e.g. CABRI [www.cabri.org] EBRCN [www.ebrcn.eu] EMbaRC [www.embarc.org]). The offer, expertise and service of mBRCs often stand in strong contrast to the attitude of scientists from academia and the bioindustry who do not take full advantage of this superior source. As demonstrated for bacteria about 70% of the reference strains used by authors in scientific studies as reference strains were obtained from peers and laboratory collections, thus of potentially doubtful authenticity. On the other hand, less than 1% of bacterial strains used in scientific communications were deposited in public collections (Stackebrandt, 2010). It is evident that the biological materials on which published data has been generated must be available to check when aberrant or erroneous results are discovered or when new technologies are available for further study and characterization. The offer of major European public service collections, combined in the MIRRI project, to accept resources during or shortly after publication is a spark to ignite the participation of other such collections worldwide. The rationale for doing so is not based on a concern that authors are incapable of short-term handling of research strains; it is based on the fact that microbial resource centres have decades of experience in handling, safeguarding and shipping a wide range of diverse material that is otherwise prone to involuntary loss by negligence or deliberate clearing of laboratory holdings. The public service collections/mBRCs comply with applicable regulatory requirements, provide material under material transfer agreements settling terms and conditions of supply and governing intellectual property in relation to international conventions, protocols and treaties. mBRCs as service collections are equipped with high expertise and technical requirements in a wide spectrum of general and applied areas which are often missing in the academic environment. Here, mBRCs can play a decisive role in complementing academic curricula by broadening the range of topics otherwise not offered by universities. It is especially the integrated analysis of complex microbial interactions, ranging from the isolation of a specimen from the environment to the description of novel species, deciphering the genomic information and its path to gene expression. Targeted identification of genes of interest for biotechnological exploitation as well as analysis of ‘microbiomes’ make mBRCs interesting partners for industry and ‘personalized medicine’, respectively. All this requires efficient collaboration between mBRCs and users from academia and industry.

The recognition of the necessity to harmonize the activities of the European mBRCs and CCs to better serve their users and to foster academic research and the bioeconomy was the initial stimulus for some large European mBRCs to apply for the MIRRI project. The positive outcome of the Preparatory Phase was seen to link additional mBRCs and CCs, as well as industrial companies as partners in a legal MIRRI entity with the mandate to support and strengthen the links and policies among them as well as between the MIRRI partners and their users. It was the ultimate aim of the MIRRI project to take the interoperability and accessibility of resources and data to a higher level, recognizing that better managed resources will lead to further discovery in all areas of the Life Sciences. Influenced
and directed by user needs, the MIRRI partners envisaged to form a network of national nodes of unparalleled depth and breadth of microbial resources, to improve access to enhanced quality microorganisms in an appropriate legal framework and to resource-associated data. MIRRI-PP focused on a selection of existing mBRCs and Collaborating Party CCs, and their resources, technologies, and expertise, which have been specifically complemented with innovative components. Based upon work started in the EMbaRC project information was collected and enriched on type and quality of collected samples and data, standardisation of procedures, IT solutions as well as authentic work of MIRRI-PP on governance structure, funding, and legal issues.

In particular, MIRRI comprised:

i) the coverage of major mBRCs whole breadth of microbial diversity, from genomic samples, plasmids, bacterial, plant and animal viruses, archaea, bacteria, filamentous fungi, yeasts, microscopic algae, protozoa, immortalised human and animal cell lines and dedifferentiated plant cell lines; the vision to deposit representative samples of microbial consortia and microbiomes;

ii) biomolecular resources, such as collections of DNA and plasmids and a variety of molecular tools to decipher information at the genetic and epigenetic level and to authenticate microbial resources,

iii) bio-computing and sample storage infrastructure;

iv) scientific, technical, educational and legal expertise; all resources are envisaged to be integrated into a pan-European distributed hub and spoke structure and properly embedded into European scientific, ethical, legal, and societal frameworks. Specific tasks during the MIRRI-PP comprised the preparation of an inventory of existing resources, achieving

• interoperability by implementation of common standards, practices and data formats,
• establishment of a strategy to harmonize acquisition to avoid unnecessary duplication of holdings
• definitions of performance indicators to measure the impact of MIRRI on BRCs, and
• provide solutions for international exchange of microbial samples and their associated data which properly consider the pertinent national and international legislation for biosecurity and ‘Access and Benefit Sharing’ (ABS).

Resources and Tools

One element of the MIRRI mission is to acquire, curate and provide live microorganisms that are interesting or valuable to the scientific, educational and business communities to foster and support the development of basic and applied science. Based on a long tradition, individual European not-for-profit mBRCs were established to allow facilitated and legal access to resources worldwide, to add value to known and yet unknown microbial biodiversity and to exploit unknown sources and knowledge to discover and disclose for the bioeconomy and bioscience generally. MIRRI is being established to provide access to the combined resource and knowledge base currently disparate and not easily connected and to respond to user needs through coordinated policy and strategy.

Microbial resources, the entire spectrum of technologies for characterization, identification and authentication and expertise to interpret the outcome of taxonomic and systematic research represent a trinity. It is therefore an overriding aim for MIRRI to assess the breadth and depth of high-quality samples, technologies, and expertise present in different European mBRCs and to coordinate these resources for innovative uptake into academic and bio-industrial research and as a result foster the bioeconomy. For optimal function of a mBRC it is necessary to coordinate excellence in all these areas in order to take full advantage of opportunities for intra- and extramural research and development. At the heart of all these efforts are the ambitions, externally (i) to facilitate access to resources and knowledge to offer solutions to the development goals and specifically the bioeconomy, (ii) facilitate user communications by providing a gate to a knowledge-based platform. Internally, within MIRRI and across the mBRC community communication will support the sustainability of mBRCs and partner collections, and improve the visibility of mBRCs as the prime source for the provision of high quality and authenticated resources under legal compliance.

In the envisaged MIRRI hub and spoke structure, MIRRI members represent the key providers of resources and technologies, to each other and to the academic and the industrial community. The associated partners and subcontractors provide resources such as services, data, samples, and materials. MIRRI WP2 had as a main purpose to define the function of MIRRI as a global infrastructure by ensuring that existing resources, services and expertise are evaluated, unnecessary redundancies removed, gaps in these facets identified and strategies developed to allow users to make optimal use of these microbial resources. However, the scope of this aim is larger than that, as with the establishment of national networks of microbial collections the range and visibility of national resources will be increased by elevating them to the European and global levels. Importantly this extends to the resource-associated data, which must be provided in a format which would allow interoperability.

The first step in the review of existing European mBRCs and resource collections for advanced use was to make an inventory. WP2 created a questionnaire to gather information on the number of holdings in public (500,000) and non-public collections (300,200). As indicated by the holder of the latter resources, 40% of these are available to the public. The questionnaire also included questions about the willingness of non-public collections to make their resources available within the frame of a future infrastructure to which 82% of collections agreed. The results of the questionnaire are available from the two Periodic Reports (http://www.mirri.org/about-mirri/project-reports.html).
The present content, scope and range of biodiversity within individual European mBRCs is due to the history of individual research projects and the history of national mandates of funding bodies. Annually, MIRRI partner collections acquire between a few dozen to up to 1,200 new strains of microorganisms, consisting of deposits of type and reference strains and of research material deposited by scientists in the community. As the criteria for deposition depend somewhat on the depositor's own interest in clinical, basic and applied research the number of resources worth depositing in public culture collections cannot be estimated. Though the deposition of prokaryotic type strains is mandatory, gaps exist for those type strains, which were either never deposited, lost by collections, or for which the description was based on dead or preserved material. The situation is different with reference strains of yeast and fungi and of non-type strains of any microbial material. Only a minute fraction of microbial strains and of genetic elements like plasmids, bacteriophages as well as purified DNA are deposited in public mBRCs. This gap in available microbial diversity is most obvious by the unavailability of strains used in the scientific literature. The missing cooperation of authors to share resources stands in contrast to the publication policy of the majority of journals which expressively states in the Instruction to Authors that biological resources included in scientific articles need to be available to the user (though not necessarily deposited in public collections). Despite the obligation to share resources, several obstacles exist that prevent putting the author's obligation into practice. Once published, most resources are either no longer maintained or are not publicly available in the long run. As the acquisition of novel material is not harmonized among European partner collections a stringent accession policy is required to guide mBRC managers and curators to coordinate a most complete offer that will satisfy the demands of users whilst balancing the needs of the individual mBRCs and their stakeholders. It was a task of WP6 to focus on the taxonomic coverage of holdings of mBRCs to assess the degree of overlap and identify gaps. The result of a questionnaire to the MIRRI Partners revealed the strength and emphasis of the microorganisms held; these could be categorized into three groups, focusing on (i) biodiversity of type and reference strains, (ii) pathogenic microorganisms, and (iii) microorganisms for applied research. Though the concentration of diversity within the narrow geographic region of Europe is unparalleled in the world there is room for improvement concerning the coordination of acquisition focus to avoid redundancy in holdings thus freeing funds for other mBRC tasks. Based upon the questionnaires of WP2 and WP6 the MIRRI accession decision matrix should focus on:

- increasing taxonomic, metabolic, geographic, and ecological strain diversity;
- reducing redundancy at lower ranks (i.e. avoiding the acquisition of genera, species and strains which are already well covered in other collections);
- resources that have been published and deposited outside public (academic and industrial) collections;
- resources which are the specific focus of innovative science and research & development;
- the provision of specialized collections, including consortia, for applications in bioindustry.

Based upon a literature survey performed in the previous European EMbaRC project the number of microbial strains cited and used in public research by academia and industry exceeds the number of annual acquisitions in public collections. It was therefore decided among the mBRC managers to suggest a policy for a pre-selection of published pro- and eukaryotic resources to be made publicly available (Stackebrandt et al. 2014). In addition, the MIRRI Accession Policy includes reasons for not accepting a resource and terms and conditions of microbial resource accession and discarding.

A Quality Management System (QMS) concept for microbial collections, founded on previous results of European projects (EBRCN, EMbaRC), has been further developed (WP3). However, the development of a specific norm for biobanks in general, including mBRCs and other public collections, will greatly contribute to attain the objective of defining common standards that a biobank needs to reach to contribute efficiently to MIRRI. The ISO Technical Committee 276 is providing the biobanks, and thus MIRRI participants, with a solution expected in 2017. The on-going work of ISO TC276, involving several participants of the MIRRI Preparatory Phase project will take the efforts regarding QMS to even a higher, internationally recognized level. In the meantime, collections will be able to gradually set up or adapt their QMS.

During the MIRRI-PP, WP2 has produced several other reports, which cover different aspects of resources and technologies available from mBRCs. One of the tasks for WP2 was to review existing European mBRC services and expertise in management, legal issues and on microbial taxa, including isolation from specific habitats, authentication methods, the opportunities for data mining and range of IT expertise. These evaluations indicated that, overall, the microbial analyses offered by mBRCs seem to fulfills user needs, except for whole genome sequence data analysis. This service could be broadened with the expertise of research laboratories as several of the non-public academic laboratories declared that they provided this analysis. In addition, several respondents specified new services that would be valuable for them, e.g. supply/preservation of microbial communities, virus propagation, training in the use of bioinformatic software, on-line microbiology courses and databases on specific taxa. It is noted that some of the “new” services proposed by respondents are already offered by public mBRCs such as plasmid typing, provision of microbial DNA, lipid analysis and species identification, thus indicating a lack of public awareness of the availability of such services.
Surveys addressing providers and users of microbial resources and meetings with these and other stakeholders served to define MIRRI. As a result, MIRRI proposes the creation of a Collaborative Work Environment (MIRRI CWE), a high quality platform for knowledge transfer targeted to both academia and biotechnology. Consisting of several gateways, offering different services; MIRRI’s CWE will answer the stakeholders’ need for an improved support of research and development in the field of microbiology. It will be unique in its scope offered to the user community.

It was another task of WP2 to define membership criteria for MIRRI in the Construction Phase. Besides the criteria imposed by the MIRRI legal structure MIRRI partners agreed a number of requisites to guarantee high quality services, proficient management and due diligence regarding the transfer and use of microbial resources. Three kinds of principles with the responsibilities and obligations of partners were identified, (i) general principles for all Partners, (ii) specific principals for mBRC Partners and (iii) principles for external partners (from non-Members and non-Observers). The respective criteria are laid down in the Partner Charter (http://www.mirri.org/fileadmin/mirri/media/Dokumente/ generalDocs/MIRRI-ERIC_Partner_charter_V7.pdf).

Governance and Operation

A key task of WP3 and a challenge during the MIRRI-PP was to find the most appropriate legal entity to support the distributed operation of the Construction Phase of MIRRI to provide access to biological samples and data that are stored and maintained in mBRCs, other public collections and non-public academic repositories. This can only be achieved by a distributed Research Infrastructure with operational units in most, if not all, European Member States. The vision of the MIRRI infrastructure including its governance structure is built around a distributed model with a hub and spokes design consisting of a Central Coordinating Unit (CCU) with a central coordinating hub (Fig. 1).

Fig. 1 Flow of information from national mBRCs through National Nodes to the CCU

National mBRCs and other resource providers and partners will channel resources, associated data, expertise and services through their National Node to the portal of the CCU. However, the mBRCs maintain their national legal status that allows them to do business independently whilst any single mBRC is an entry point to the infrastructure. The Central Coordinating Unit as the executive body will execute the directives of the Assembly of members, and it will deliver the annual work plan for the Directors’ Forum and mBRC members who will respond individually to their users.

The activities of the executive body (Executive Director and CCU) will be defined and governed by the decision making Assembly of Members. The Assembly of Members consists of delegates of all members of MIRRI-ERIC and of officially endorsed Observers, guided by an Advisory Board (Fig. 2) for Ethical, Scientific, Legal and Industrial issues. The scientific Advisory Board will ensure user benefits are delivered from the improved quality management of mBRCs and better access to authentic and reproducible materials in a transparent and traceable way.

Fig. 2. Envisaged path of directives owing from the decision-making bodies via the executive to the operative level within a MIRRI legal entity

The Assembly of Members would appoint an Executive Director who would be independent of any mBRC. Speakers of the ‘mBRC Directors Forum’ and the ‘National Coordinators Forum’ (National Nodes) groups would be elected to work with the Executive Director, who has the mandate to direct them within the scope of the membership criteria. Specifics of the interactions between the individual bodies are laid down in the MIRRI Statutes. The mBRC Directors Forum consisting of all directors of the signatory Partner-mBRCs of the MIRRI Partner Charter, shall discuss and conclude on an annual update of the common accession policy and make adjustments when deemed necessary (e.g. new member mBRCs, or new taxa and properties described). According to the MIRRI Partner Charter, mBRC partners agree to a targeted accession of biological material to broaden the range of strains that are of high interest to bio-industry and academies. These updates shall be included in the Annual Work Plan to allow the Executive Director of the Central Coordinating Unit to coordinate its implementation through national nodes.

The composition of the CCU will include the Executive Director, IT, Science officer and communications/customer relations officer. The Central Coordinating Unit will be responsible for:
- Managing the technical aspects of mBRCs
- Coordinating the infrastructure with other international initiatives
- Providing an intergovernmental forum on mBRC issues
- Project development and management
- Technical issues for membership
- Outreach and publicity
- Organisation and delivery of capacity building programmes
Central financing issues

The envisaged legal MIRRI structure

EU research infrastructures require a specific legal shell to accommodate either diverse national regulations or European rules. The legal status must provide a guarantee concerning the liability, the financial control and the human resources management and it must also support the governance structure. Based upon a thorough evaluation of existing legal structures the European Research Infrastructure Consortium (ERIC) status was early on identified by the MIRRI consortium as the mechanism of choice to facilitate multi-state funding. Therefore, the internal policy and the governance structure would be designed together with representatives of State Governments and other relevant stakeholders. The operational structure for MIRRI in the Construction Phase (WP2 and WP3) was designed to include the elements necessary to comply with the MIRRI-ERIC. The MIRRI Statutes were agreed, which lay down the principles on which MIRRI will be founded. To facilitate the establishment of MIRRI a MoU or other forms of short agreements which express a States’ interest in supporting MIRRI financially and establishing a coordinating centre has been drawn up. These States will work together to establish the legal entity and enable MIRRI to become operational. In a joint effort coordinated from MIRRI, each partner will seek the engagement of their respective relevant national authorities to participate in this process.

To date five States have signed the MoU (France, Greece, Latvia, Poland and Spain). While most representatives of the first two meetings with national representatives did not object against the establishment of an ERIC, stakeholders of other states not yet having signed the MoU, recommended alternatives. As, however, MoU signature States have not yet met to discuss the future of MIRRI, neither a decision on the legal structure nor on the finalization of MIRRI Statutes and Rules of Operation have been made. This being the case, the term MIRRI-ERIC will be used to denote the legal structure in the Transition and Construction Phases until the final decision is taken by the State representatives.

Funding and financing

As laid down in the MIRRI Partner Charter, mBRCs agreed to contribute to MIRRI with defined elements of their business. Each Member State will be asked to establish a National Node to coordinate national networking activities. These two MIRRI elements, as well as the personnel and infrastructure of the hub (CCU) require public support. In order to develop a funding concept the impact of harmonised organization of mBRCs was evaluated. Existing funding schemes of MIRRI partners were not included in the long-term funding scheme of the MIRRI-ERIC as most of the individual mBRC activities run outside MIRRI and each national mBRC is financed in a different way and by different funding bodies. MIRRI concentrates on coordination of activities rather than of coordination of funding. The reason for this is that currently mBRCs often waste resources due to duplicated efforts, e.g. by independent development of IT-solutions, duplicated acquisition of resources, introduction of expensive instrumentation or by independent implementation of different standards and quality assurance measures. For full implementation of a MIRRI-ERIC, to achieve cost effectiveness and for securing long-term operation, increased investments into these key resources must be made:

- to improve efficacy and quality of research in the field of life sciences,
- to improve research & development,
- to unravel the hidden potential of microorganisms,
- economic issues, and
- regional development.

The information collected by MIRRI and previous EU-funded projects has been used as the starting point for the development of long-term funding concepts, for MIRRI, which considers the whole spectrum of funding schemes including national, European and private funding organizations. The MIRRI funding concept as it has been developed and summarized in the three iterations of the MIRRI Business Cases and further updated based on national stakeholder input.

Each of the three iterations of the MIRRI Business Case previously reported on, has been progressively strengthened as more is developed on the structure and mechanisms of MIRRI operations and the true cost of the Central Coordinating Unit (CCU) estimated. Overall, the MIRRI approach assumes a not-for-profit model sustained by mixed funding; implying long-term core support by participating Member States and income generation through centrally coordinated activities. The balance between core support and income generation is projected to evolve as the consortium is constructed and as operations (including income generation) come on stream. As a result of national representative meetings, the financial projections and costs have been modified with the latest model designed to reduce Member State contributions to 10% of their original contribution at year 6. There are two distinct cost centres, the MIRRI-ERIC implemented by the Central Coordinating Unit (CCU) and the second around National Nodes (NNs) and their networked mBRCs; it is only the former that can be adequately addressed at this time. The cost for establishment and operation of National Nodes along with the enhancement and participation of the national mBRCs affiliated with them is dependent upon a number of factors. These include the number of mBRCs participating, the degree of development and maturation of the node, the extent to which mBRCs have devolved some of their activities to a central unit and local costs. This is a national obligation outside the costings for the MIRRI-
as well as further innovations in the life science industry will strongly depend on transnational access to high quality microbial...cutting edge research involved them into the development of the planned infrastructure a meeting with R&D experts made it clear that the MIRRI offer, in order to provide a positive contribution to a contingency fund. A risk analysis and contingency plan is in place providing a robust basis for these financial projections. Already MIRRI has had success in securing project funding in H2020 totalling around €1.7 million for various activities; potentially 10% of this would be functions that the MIRRI CCU could provide. Therefore, it is the intention that MIRRI will be 90% self-funded at year 6 (Fig. 4).

Fig. 4 Distribution of income streams in year 1 and year 6 of MIRRI-ERIC

Communication, dissemination and outreach
Being on the ESFRI Roadmap with 12 sister initiatives, it is important to avoid duplication of efforts and waste of resources. Therefore, synergies and shared strategies with the other projects from the ESFRI Health and Food Group were analysed (WP5). MIRRI complements the framework of this group and is a dedicated partner in several European cluster projects (CORBEL, EMBRIC, Ritrain). Existing contacts to related initiatives beyond Europe were nourished and MIRRI is meanwhile a well-known initiative around the globe. During the Preparatory Phase, several communication and outreach instruments (WP5) were successfully established: the public website incl. a password-protected area for project-internal communication, a regular electronic newsletter (with more than 1,100 recipients), well-accepted social media accounts (Facebook, Twitter, LinkedIn, Google+), several flyers as well as a short animation film introducing MIRRI to the naïve stakeholder. In addition, regular representation of MIRRI at international high-level conferences, a set of peer-reviewed MIRRI publications and - via Zenodo - publicly accessible deliverables and policy documents round the outreach activity during the Preparatory Phase.

Each of the MIRRI Partners and Collaborating Parties have, since their establishment, developed individual links and communication channels with their user clientele and national stakeholders, mainly funding bodies. Due to confidentiality clauses, the names of users from the bioindustry cannot be disclosed while the names of users from the academic environment are often visible from published studies in which the accession numbers of microbiological resources allow the identification of the providing mBRC. There was general agreement among the MIRRI consortium that each mBRC will stay independent in addressing user needs which originate mostly from within the country the mBRC is located in. Only the large mBRCs have a more international, even world-wide user clientele from the academic and industrial sectors. One of the main objectives of WP5 was the development of improved communication tools to convince users to rely on authenticated resources and to recognize the added value in receiving resources with a plethora of associated data and links to expert knowledge. A second objective was to ensure appropriate communication to external stakeholders as well as project-internal exchange of information. The output of the six tasks of this WP resulted in an overall MIRRI Communication and Outreach Strategy.

An extended stakeholder analysis was performed, identifying 26 relevant stakeholder groups of MIRRI and their individual ‘stakes’ in the project. Based on this information a customized outreach for the different stakeholder groups was developed. In collaboration with WP2, an online survey was conducted, focusing on the identification of opportunities to improve the communication between resource providers (i.e. mBRCs) and users. The main results show that mBRCs should promote their offers (resources as well as services) more actively as many of the researchers are not aware that mBRCs act not only as providers of resources but also of technical services. In addition, to keep up to date with the market demand, mBRCs need to be more active in asking clients for their expectations. A first step towards improvement of this communication was the provision of a) links to the online catalogues of MIRRI participants and b) a list of services offered by them on the MIRRI public website. The industrial users are one of the main stakeholder groups for MIRRI and to involve them into the development of the planned infrastructure a meeting with R&D experts made it clear that the MIRRI offer, in order to attract these stakeholders, needed to be articulated more clearly and targeted to the needs of the bio-industry. Cutting edge research as well as further innovations in the life science industry will strongly depend on transnational access to high quality microbial...
resources and associated information for academia and industry in an efficient and secure manner. Furthermore, microbial resources are a key resource underlying a series of legal restrictions thus requiring a harmonized solution for efficient usage (WP9). The major goals addressed are:

1. The level of interoperability of resource-associated data that can easily be retrieved by industry for further product development and to foster R&D;
2. Facilitating access to foreign resources in full compliance with the Access and Benefit Sharing Articles of the Nagoya Protocol and the Convention on Biological Diversity;
3. Fostering access of the industrial user to mBRCs and vice versa to exchange experience and allow training under confidentiality clauses;
4. Establishment of ‘MIRRI Expert Clusters’ as one of the elements of the Collaborative Work Environment (CWE) platform. These Clusters will consist of mBRC staff and external experts from Academia and the Bio-industry, responsible for responding to all questions around basic and applied research on resources, including legal compliance issues. MIRRI Expert Clusters integrate pre-competitive public and private research and development activities by providing scientific expertise related to the resources and their data. Thus the establishment of Expert Clusters communicating with all other elements of a CWE creates a win-win situation for all parties by:
   • enhancing collaborative research;
   • using limited resources efficiently;
   • increasing the knowledge base;
   • sharing data, technology, knowledge and expertise;
   • facilitating innovation;
   • increasing competitiveness in academic science as well as at the marketplace through product innovation.

Education and training

One MIRRI partner (UMinho) has participated in EMTRAIN and is currently participating in Ritrain project training program of the IMI (Innovative Medicines Initiative). The aim has been to coordinate the different training activities at masters’ and doctoral levels in the different Member States. EMTRAIN aims to establish a training syllabus for professional scientists in the different aspects of drug development and MIRRI will be an important contributor to such a training program.

In order to produce a coherent strategy for Education and Training (E&T) activities, including new tools for training and an innovative learning programme to implement in MIRRI, Task leaders and contributors of WP7 have gathered information from the literature, available legal and administrative documents, surveys, and interaction with other projects such as Lifetrain. This information was integrated and discussed among project members, aiming to bridge identified offer-demand gaps, update, harmonize, establish accreditation and coordinate the E&T offer.

Briefly, a strategy and mechanisms for implementation of the MIRRI E&T offer were discussed, designed and described. The prominent role of not only the individual mBRCs but also of the CCU in coordinating liaisons with stakeholders and Higher Education Institutes (HEI) was outlined. The MIRRI CWE will provide a compilation, organize and advertise the E&T offer. Appropriate steps will be taken to assign European Credit Transfer System (ECTS) credits for achievements or ECVET (European Credit System for Vocational Education and Training) points for qualifications, aiming to standardize certification of the E&T offer and promote knowledge and staff transfer between mBRCs, academia and industry.

A workshop was organised to discuss the relevance of mBRC activities and mandates to society, promote coordination thus reducing fragmentation, and to identify aspects of microbiology that are under-represented in academic curricula to provide a base for bridging gaps. A strategy was discussed that would focus on species richness, traditional taxonomic determination tools as well as modern -omics related content, bioinformatics and databases. With the coordination of the CCU, and organised via the CWE, a set of alternative, but not exclusive, strategies can be put in place, all of which require the dedication and involvement of the mBRCs: E&T dedicated to stakeholders and users and mBRC staff itself through CPD; a selection of E&T activities to be included in a catalogue for summer schools/MIRRI Academy; and, in close connection with HEI, the incorporation of the MIRRI E&T offer in academic curricula.

Database management, biocomputing and IT interoperability

During the MIRRI-PP, WP8 planned and coordinated the interoperability of the existing databases of mBRCs. Based on this planning work, the IT-infrastructure of MIRRI-ERIC will be created and will consist of a network using the hub-and-spoke topology to connect the different nodes. Nodes are independent entities from mBRCs and other public collections and channel the distributed information on resources, associated data, service and expertise offer to the CCU. Based upon strategies devised in previous EU projects, information harmonization will primarily utilize a minimum set of data attributes, which are assumed to be achievable by all microbial collections. mBRCs are encouraged to provide additional data, including data from the scientific literature, to enrich data value and utility, and links to external databases. Use of the system for data discovery will be the first step towards complete data federation.
The objectives of WP8 were to define concepts and strategies to improve the quality, quantity, interoperability and usage of data associated with biological material in mBRCs. The objectives were reached by conducting four workshops and satellite/SC/WP meetings with internal (MIRRI) and invited participants as well as a survey on user requirements in terms of deposition and access to data provided by MIRRI. This has resulted in a detailed picture of the current data management and ICT infrastructure in mBRCs. Most mBRCs are acting as proprietary entities with respect to data acquisition, data quality management, data exchange and interoperability. Despite the fact that ‘OECD Best Practice Guidelines for Biological Resource Centres’ and CABRI guidelines for minimal datasets exist, standardized protocols for submission and insertion of strain specific associated data (metadata) to mBRCs have not been commonly implemented. Heterogeneous and incomplete datasets in mBRCs are the consequence. Furthermore, the lack of commonly agreed exchange formats as well as heterogeneous and often insufficient ICT-competences hamper data exchange and interoperability between mBRCs as well as third party databases. As a consequence, the usage of the accumulated knowledge stored in mBRCs is hampered for stakeholders in academia and industry. Improved access to biological materials and its metadata is clearly needed. The current situation results in different data exchange formats for services such as www.straininfo.net/ that uses a published microbiological common language (Verslyppe et al. 2010) whilst the Global Catalogue of Microorganisms requires a somewhat simpler excel spread sheet based exchange of data (gcm.wfcc.info/). There are several systems requiring different datasets in different formats doing related things making the mBRC task overcomplicated and leaving the user confused.

A way forward was outlined based on user feedback and workshop participant discussions to establish the MIRRI Information System (MIRRI-IS). MIRRI-IS will deploy an integrated, high-quality, manually annotated, non-redundant micro-biological resource database which provides all relevant information data and associated contextual data (metadata) about a particular biological resource as part of the MIRRI CWE. MIRRI will work with its partners including other ESFRI research infrastructures, to link its mBRC data to other relevant data sets facilitating the generation of knowledge from data. It will provide high quality, well curated strain data to enable discovery of new products and properties and drive innovation in microbiology. Innovative links to ecological (substrate and habitat), genomic and chemical properties and metabolic pathways to taxonomic and environmental relationships will facilitate the user locating microbial resources to enhance their studies and find new leads and products.

The current status as well as the strategy to move forward has been detailed in the strategy paper “MIRRI WP8 strategy paper about data resource management”. The paper summarizes the current status of data management in mBRCs as well as the vision for the MIRRI Information System as an integrated, high-quality, manually annotated, non-redundant micro-biological resource database. The MIRRI policy on data management (http://www.mirri.org/downloads.html) highlights the need to overcome the current fragmented situation by establishing the MIRRI-ERIC Information System as part of the Collaborative Work Environment (MIRRI CWE). MIRRI-IS will be designed as the central entry point for users, curators and developers that need access to the integrated knowledge of mBRCs and selected third party databases while assuring that the specific competences of partner mBRCs remain transparent. The aim is to establish a trademark for high quality data and expertise, which enhances the reputation of participating mBRCs.

To allow MIRRI-IS to be operational, MIRRI partners need to comply with:
1. Machine-readable mBRC catalogues by providing data in a structured electronically available format; over time, each mBRC in MIRRI should provide their data by Web Services in an XML based exchange language, e.g. based on the Microbiological Common Language (MCL) and its extensions.
2. The digitalization of key information that is not yet digitally available;
3. Provision of accurate data;
4. The MIRRI Minimum Data Set (MIRRI MDS) of descriptors which include a few basic, but absolutely necessary, sets of information on data in order to be compliant with the EU ‘Access and Benefit Sharing’ regulation. Besides these fundamental fields, specific “data packages” and additional subfields will be added over time to enrich the MDS. This will be extended towards a recommended (RDS) and eventually full data set (FDS);
5. The content of the fields is expected to follow the guidelines, data model, controlled vocabularies and ontologies specified by the MIRRI consortium;
6. The final set of fields, including their expected content, will be consolidated in the Minimum Information about Biological Resources standard and checklist;
7. Curation level and quality of data needs to be assured by unified Standard Operating Procedures in mBRCs;

A detailed summary paper: “An Information System for European Culture Collections: the way forward” (accepted SpringerPlus-PLUS-D-15-01351R1 [EMID:24a5ef8efb9ddf50]) lists and discusses informatics infrastructure needs for mBRCs, their curators, associated technicians, researchers, clients and end-users.

To force the implementation of a common working environment among mBRCs the WP8 “Commitment to a FAIR (Findable, Accessible, Interoperable and Reusable) provision of data and information to meet MIRRI's data management (WP8) and delivery need” have become part of MIRRI's Partner Charter.
Legal operational framework

MIRRI-mBRCs are expected to adhere to European and national laws. With regard to utilization of genetic resources and traditional knowledge associated with these genetic resources over which countries of origin have sovereign rights, mBRCs are in a position to educate scientists, including depositors of genetic material, on the provision of the required documentation to comply with national and international law. An ‘Access and Benefit Sharing’ (ABS) Manual (http://www.mirri.org/downloads.html) has been prepared by WP9 to assist the mBRCs implement institutional ABS management policies governing daily practices for accession, research and transfer of material by all staff. In the Manual MIRRI lays down best practice providing a light general policy, leaving the detail of the mechanisms of compliance to the discretion of individual MIRRI-mBRCs.

The MIRRI-ABS policy statement (https://zenodo.org/record/47247#VOWy4VJuJkQ) applies to all mBRC holdings and other biological materials, in public and non-public collections including, but not limited to, living cultures, dried herbarium specimens, dead wet samples, DNA samples and other derivatives of biological material, as well as traditional knowledge and scientific data that are associated with these resources.

More specifically, the MIRRI-mBRCs are committed to:

1. contribute to the conservation of biological diversity through the preservation and study of ex situ microbial materials and genetic resources thereof, or the encouragement and promotion of such study by others, in accordance with Art. 9 of the CBD;
2. deliver, in compliance with the CBD, the Nagoya Protocol and all applicable legislation and regulatory requirements, well-identified, authentic and high-quality materials that are preserved in the public collections of the mBRCs to third parties for research and development, education and biotechnology, and data associated with these resources, to the benefit of public health, food security, and social and economic development. In doing so, the mBRCs also contribute to the Nagoya Protocol’s wider objective of supporting the conservation and sustainable use of biological diversity;
3. present clarity on permitted use to recipients of ex situ microbial genetic resources, considering that these resources are the essential raw materials that drive the bio-economy, and while fully recognizing the sovereign rights of the countries of origin over their genetic resources, to refrain from posing unnecessary restrictions upon the use of these resources in research with commercial intent, while reminding users of applicable benefit sharing obligations through transfer agreements;
4. cooperate with relevant associations of users and other interested parties in the EU and globally to develop procedures, tools or mechanisms that can facilitate the implementation of the Nagoya Protocol, stimulate the use of ex situ microbial genetic resources, and lead to an increase in transparency and legal certainty or a reduction in costs for both provider mBRCs and the users of the microbial genetic resources;
5. design a practical and transparent legal framework that includes transfer agreements with model clauses, and best practice under which all MIRRI-mBRCs can operate as far as is permitted under applicable national law;
6. respect, where appropriate, the confidential nature of user information, documentation and administration associated with the transfer of microbial genetic resources;
7. put institutional policies or other measures in place which assure that the mBRC staff act with due diligence and in full compliance with applicable national and international ABS law and regulatory requirements, in all collection management activities, when collecting new biological materials during fieldwork, or conducting research;
8. inform stakeholders in general about their rights and obligations concerning ABS, where appropriate;
9. share benefits arising from the utilization of the genetic resources by the mBRCs themselves, with the country of origin and other rightful stakeholders, in accordance with the provisions of the Nagoya Protocol and applicable legislation or regulatory requirements, where appropriate, and including, but not limited to,
   (a) adding value by generating new information on the characteristics of the genetic resources preserved in the mBRC’s collections, and where appropriate make this information publicly available through scientific and popular publications and by adding information to open access data repositories;
   (b) providing support to initiatives for the establishment of new ex situ collections in developing countries through collaborative research programs, training and other means of sharing expertise.

A second aspect of the legal framework for access to microbial resources relates to biosecurity assessment. Microorganisms have been harnessed for the benefit of humankind but in the wrong hands could be used in direct or indirect acts against humans, livestock, crops, food, water infrastructure and other economically valuable entities. The life science community is a key stakeholder in the effort to ensure that the advances in biotechnology are not misused for hostile purposes. Unfortunately, to date, the engagement of life scientists with issues of biosecurity has been limited. The MIRRI-PP has addressed the topic implementing a Code of Conduct as part of its program of prevention of malicious use. Biosecurity has become a major concern for several countries creating numerous
activities to put in place counter measures, risk assessment, legislation and emergency response. The goal is to implement measures to protect us against malicious use of microorganisms, their products, information and technology transfer. Effective Biosecurity risk management is more than reliable and appropriate risk assessment. It also involves assigning responsibilities to members of staff and communication to (internal) staff and third parties (users). In this context, awareness raising is the most fundamental basis for implementation of biosecurity and requires educational programs in the future in order to communicate broadly what biosecurity is and why biosecurity measures are demanded. MIRRI's policy will capture this and also addresses the issue in its training and education offer.

The key elements of the MIRRI policy on biorisk management in mBRC (https://zenodo.org/record/47248#VOW1E1JuJkQ) is to
1. follow the relevant national law adhering to
   • the Code of Conduct on Biosecurity for BRCs
   • other comparable recognized standards
   • OECD Best Practice Guidelines on Biosecurity for BRCs;
2. follow the development of biosecurity implementation strategies and adjust practice accordingly;
3. work in collaboration with MIRRI- and external partners towards developing and implementing protocols for adequate biosecurity risk assessment of holdings and normative compliance in MIRRI-mBRCs;
4. offer available specific expertise to the MIRRI biosecurity expert cluster;
5. work with national authorities to increase competence and advocate the establishment of national biosecurity offices and their international cooperation;
6. work in collaboration with MIRRI- and external partners to strengthen the ethical basis for biosecurity in the scientific community;
7. adopt existing or develop new educational tools to raise awareness among mBRC staff;
8. work in collaboration with MIRRI- and external partners to strengthen the ethical basis for biosecurity in the scientific community;
9. adopt existing or develop new educational tools to raise awareness among mBRC staff.

Potential Impact:
The availability of authentic microbial resources, maintained under conditions under which the least chance of genetic modification occurs, is one of the prerequisites for a sound and reproducible science in microbiology. Microbiology is one of the cornerstones in biological science, with huge impact on 1) basic research (such as the evolution of life on Earth), 2) understanding processes (such as global cycling of gases and waste) at the genetic and epigenetic levels and 3) the bio-economy (such as fundamental resources for social and economic prosperity and Health). Any country in Europe with its unique diversity in landscape, geography, climate and life forms has access to a likewise unique microbiota, ranging from microorganisms to their subcellular parts. Preservation of such diversity has been recognized for more than 120 years but the issue has been elevated to a global level recently by the notion that countries have ownership over their biological resources (Nagoya Protocol and the EU Regulation 511/2014).

Though the goal to improve the credibility of science and the levels of food production and population health is important for any government, the differences in preserving and maintaining microbial diversity vary quite distinctly within European Countries. While some countries have a long tradition in recognizing the intrinsic value of certain parts of the microbial diversity and cover a fragment of diversity in depth and breadth, other countries have less experience and started only recently to cover a small and defined spectrum of microorganisms which serve the countries’ immediate needs in certain aspects of their academic education, bio-economy and health. As a consequence, the landscape of European public mBRCs is fragmented, containing gaps as well as overlap in holdings. Access to good quality microbiological material is an important determinant to guarantee socio-economic equalities in science and applied research involving microorganisms. By placing MIRRI on the ESFRI roadmap, EU Member States have identified the need to ensure reliable access to diverse and high quality microorganisms as a priority. This goal can only be achieved by finding a strategy to harmonize the different national mandates and to bundle the strength of individual mBRCs and national networks in technological approaches, expertise and educational skills through a central Portal (MIRRI CCU) to maximize mBRCs’ efficiency, to respond to national challenges, hence to enhance European competitiveness.

A legal MIRRI entity will provide the infrastructure to rectify the shortcomings of the present situation by providing solutions for transnational harmonized access to resources, their associated data, services and expertise to respond to needs of users from the academic, health, agricultural and bio-industrial sectors.

MIRRI in its Preparatory Phase involved 16 Partners and 28 Collaborating Parties from 19 European countries (www.mirri.org/consortium/partner.html) which underlines its pan-European scope.

Nevertheless, among the institutions involved there is a significant dominance of Western European Member States. In the context of implementing the European Research Area and European Cohesion Policy MIRRI-ERIC further promotes participation of new Member States with its distributed architecture, by the adoption of the ERIC legal framework, and a series of specific stimulation programmes. The description and classification of the diversity of species signalled the beginning of scientific research on living matter. When in 1735 Carl von Linné published his taxonomic work on the Systema Naturae, his ideas about a new order of nature triggered a
revolution, which above all shaped biology for a considerable time. Almost 280 years later, it is systematics, meaning the discipline of the monitoring, description and classification of biodiversity that forms the important basis of almost all research areas in life sciences, hence the cradle of the first microbial collections. Passing through periods in which firstly morphology and then physiological traits were considered important for taxonomy; today, through the introduction of high-throughput analysis for molecular information, the -omics revolution has changed the science of microbiology, though not exclusively so, at an unprecedented pace. Hitherto hidden diversity and the complex interactions in our environment are unravelled. Scientific advances on taxonomy and the accurate testing tools for identification of biological material have permitted the differentiation of closely related organisms that may have very different functional roles and interactions. Such advances have, for example, come up with useful diagnostic approaches that have allowed the identification of non-pathogenic or non-toxicigenic organisms that belong to groups that are generally recognized as safe (GRAS). This has vast implications for health (clinical diagnostic), bioindustry (quality control), and crop protection (species complex, patho-types) sectors.

A new modern taxonomic scientific discipline emerges which more than ever is defined by its integrative character. These changes are associated with huge challenges which science and society face in order to utilize the potential of a modern holistic discipline of systematics. A legal MIRRI Consortium offers solutions to how the public mBRCs can be involved in the process of bringing together the hitherto fragmented elements to approach the complex quest of understanding biodiversity.

The science of studying biodiversity at the international level must be enhanced through a number of measures, such as prioritization, resource and data networking, strengthening of education and development of research infrastructures. MIRRI will participate in achieving this goal through the following six measures:

1. Creation of centres of excellence, in which dedicated MIRRI partner mBRCs and university(ies) foster research and education. All MIRRI Workpackages were defined to reach this goal.

2. Creation of a competent infrastructure for integrative biodiversity. The taxonomic strength of European MIRRI partner mBRCs and academic institutions should be linked to remove gaps in education and training. The emerging network should be a direct contact partner for policy and societal issues, should through its Central Coordinating Unit coordinate and identify mBRC-specific research and harmonize processes for standardization at the national and international levels. The establishment of a Cooperative Work Environment with individual gates to expert clusters is presently under implementation.

3. Creation of competitive research infrastructures dependent upon peer reviewed strength in technology and expertise. Existing focus on molecular know-how, isolation of the hidden biodiversity and technologies with relevance for the bio-industry should be strengthened.

4. Creation of international linkage of resources with data to accomplish an integrative biodiversity platform, at the most modern methodological and technical level. MIRRI has tested different IT solutions and datasets to find the present optimal solution. Linkage to other European data infrastructures and national data centers is envisaged.

5. Outline a strategy for an Open Access to published data by liaising with publishers, to provide access to future and older taxon descriptions, ecological, molecular and phenotypic data. This also includes the transfer of written mBRC-internal records into an electronic format under a common standard. Internationally available knowledge in biodiversity, taxonomy and systematics should be made available by means of open access publication, linked open databases and educational curricula in order to facilitate knowledge transfer on biodiversity, systematics and curated holdings data.

6. Creation of a knowledge-based platform on which experts with knowledge in education and research in biodiversity and mBRC intrinsic expert knowledge meet to coordinate links to Universities.

MIRRI-PP provided essential resources and technologies to support several of Europe’s grand societal challenges, and consequently, will be a fundamental component in addressing the ongoing and future requirements particularly of the EU’s competitiveness and innovativeness in biotechnology related industries. mBRCs will provide a framework where public financial resources as well as expertise and technologies from academia and industry can be integrated to speed-up collaborative research and to perform analyses of samples under legally compliant conditions by exploring new models for interactions between the provider and user of microbial resources. The MIRRI-ERIC will further enhance the coordination and develop synergies between these infrastructure components by creating a unique body of expertise with the capacity to make such improvements. This will be facilitated and made accessible by establishing a Collaborative Work Environment (MIRRI-ERIC-CWE, see Fig. 5), in which traditional on-site capacities are transferred into a virtual work environment to meet comparable offers and be linked to supporting capabilities regardless of their geographical provenance. This means that a complementary and enriched range of services and products can only be provided to the users by applying different dissemination, search and collaborative tools. The MIRRI Collaborative Work Environment will be operated by the MIRRI-hub supported by MIRRI partners from mBRCs.

Figure 5: Scheme of the envisioned MIRRI Collaborative Work Environment (CWE)
The functional part of the CWE will be gates to 1) network & project information, 2) data & resources, 3) collaboration & experts and 4) training & education. MIRRI attempts to remove barriers that obstruct the users’ view on a global offer of microbial biodiversity data and beyond, linking these data from ecology, climate, human, animal and plant health and more. Thus MIRRI through its CWE creates a culture of transparency and empowerment. The Information and Communication Technology (ICT) Systems to be used to develop a functioning CWE can fundamentally transform knowledge transfer in science, society, economy and all our current institutions. According to Dirk Helbing (http://papers.ssm.com/sol3/papers.cfm?abstract_id=2539330) ICT in the biological domain have the potential to change traditional institutions specifically in the way they educate (personalized education), the way research is done (Big Data analytics) and to add tools to e.g. the health system (personalized medicine). As part of Economy 4.0 creating a Digital Society the MIRRI-ERIC-CWE will create new solutions to persistent problems, draw together innovation, expertise and insight from sectors that have traditionally been isolated from one another and to align interests to increase shared value. In the same way Economy 4.0 and the Digital Society shape a Participatory Market Society, MIRRI-ERIC will develop into a Participatory Research Infrastructure.

In terms of legal compliance, Europe cannot act independently and MIRRI-PP has taken a leading role in discussions with legislators (EU Consultation Forum) and national authorities on important issues of the EC Guidance documents on the implementation of the Nagoya Protocol in Europe. Minimal requirements for enhanced compliance by mBRCs to the Convention of Biological Diversity and Intellectual Property issues were determined, and a MIRRI Policy and Best Practice on Access and Benefit-Sharing (ABS) developed. An International MIRRI-Workshop on Best Practice for Access and Benefit Sharing (September 2015) was attended by representatives of the European Commission, national competent authorities and national focal points, CBD Secretariat, MIRRI partner mBRCs and several international stakeholders to discuss the implementation of the Nagoya Protocol and the EU Regulation 511/2014. A MIRRI roadmap for ABS and subsequently an ABS Manual offering guidance for mBRCs were provided; the latter of which can support microbiologists within and outside MIRRI with their ABS implementation.

MIRRI addressed biosecurity implementation and compliance in mBRCs, with a special focus on biosecurity risk assessment. The results of a Workshop “Biosecurity Implementation Strategies and Compliance Management in mBRCs” (December 2014), attended by experts representing the user community, governments, industry and MIRRI partners, led to a biosecurity roadmap for MIRRI, a policy statement on bio-risk assessment and management and a strategy designed for the implementation of biosecurity measures in mBRCs.

It is envisioned that these efforts will specifically include the Eastern and Northern European countries, which have recognized a clear need in this regard. Moreover, they will be internationally networked beyond the EC (links have already been created with East Asia, Africa and South- and North America) to leverage the European position in a global context. In order to refine the concept of this future European infrastructure a MIRRI Workpackage focused on communication & PR to develop dissemination activities and a public communication strategy. On the one hand, the communication strategy addressed the common aspects of all life science (BMS) infrastructures, emphasising the momentum generated by these infrastructures to increase competitiveness of European science and industry.

Establishing a Common Windows Environment (CWE) will be the key to build the European microbe infrastructure, which will be a component of the Digital Society. Building on MIRRI-ERIC, it will be important to create a European effort and associated infrastructure to coordinate and foster cooperative initiatives that integrate existing microbial resource centres, and advanced basic and applied microbial research resources in both academia and industry. The clear focus is on maintaining already preserved diversity with attempts to acquire novel microbial resources with value to basic research and applied economic benefits and health. Microbial strains must not be seen as stand-alone resources but one component of an integrated system that link past and future published data of the entire spectrum of basic and applied research to predict novelty and hidden values of the raw material for innovations and growth of the bio-economy.

References

List of Websites:
Public website: www.mirri.org