



# **Biological and Medical Sciences**

## **Thematic Working Group**

### **Report 2010**

© European Strategy Forum on Research Infrastructures, 2010

Contact:  
ESFRI Secretariat  
Postal address:  
European Commission  
SDME 01/128  
B-1049 Brussels, Belgium  
Tel: +00 32 2 299 25 39  
Fax: +00 32 2 299 21 02  
ESFRI@ec.europa.eu

[www.ec.europa.eu/research/esfri](http://www.ec.europa.eu/research/esfri)



European Strategy Forum  
on Research Infrastructures

# **Biological and Medical Sciences Thematic Working Group**

## **Report 2010**





## PREFACE

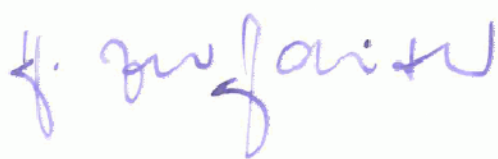
Investment in research, education and innovation is crucial to ensure Europe's ability to meet current and future societal challenges characterised by global change and the growing international competition. Research and education increase Europe's competitiveness and promote its sustainable and resource-efficient economy. Therefore the primary goal of the Member States of the European Union is the strengthening of the scientific and technological basis.

The urgency of the important societal issues requires remarkable efforts to bring together the critical mass of expertise and resources, to integrate and structure them - which cannot be made solely by individual countries. In this context, Research Infrastructures play an essential role in the research-related policy for they substantially contribute as a strategic element to the necessary structural, organizational and personnel requirements for internationally leading research and innovation.

Only if Research Infrastructures are involved in the dynamic developments of the research areas, can they become highly attractive for the best researchers from academia and industry by a continuous adaptation to the requirements of the specific fields. Both a high efficacy associated in the training of scientific and technical talents and a strengthening of the relevant research and innovation location will be combined by these dynamic developments.

An open and fair access is essential, regardless if the Research Infrastructures are rather basic- or application-oriented, single-sited or distributed. Research Infrastructures are elementary actors for the development of key technologies and the pooling of know-how in the various disciplines. The integration of hitherto isolated established resources in the relevant research and innovation scene accompanied by harmonisation and standardisation contribute significantly to a fruitful effect on the respective boundaries of disciplines and locations beyond.

ESFRI has performed highly valuable work for the Life Sciences in recent years by the identification of needs for Research Infrastructures in the field of Biological and Medical Sciences and by paving the way to their implementation. This beneficial development must be continued.



Harald zur Hausen

Nobel laureate



## FOREWORD



The Biological and Medical Sciences Thematic Working Group (BMS TWG) is proud to present the 3<sup>rd</sup> edition of the BMS Report to ESFRI Forum and the scientific community.

In March 2009 ESFRI Forum decided to limit the call for new proposals for the ESFRI Roadmap (RM) to the areas of Energy and Biological and Medical Sciences. In addition, all Thematic Working Groups in ESFRI were asked to give a strategic view on:

- The respective scientific landscape of Research Infrastructures (RIs) in Europe
- The RIs on the ESFRI Roadmap
- The future role of ESFRI in a changing ERA

To capture this strategic view of the European RI landscape, BMS TWG has drafted a landscape that encompasses and extends beyond the ESFRI process, towards realisation of the goals of the European Research Area (ERA). BMS RIs, in forming the framework of one important pillar of ERA, the **European Research Infrastructures Landscape (ERIL)**, will facilitate the emergence of Europe as a centre of competitive research excellence with a thriving knowledge economy embedded in an open innovation environment. BMS TWG introduced the term ERIL to help improve the visibility of ESFRI and to best describe one of the main achievements of ESFRI.

While only two ESFRI areas, Energy and BMS, were open to receipt of new applications, ESFRI received a number of infrastructure applications for this limited call that did not fall into either area of research. This is a clear indication that the scientific community views the ESFRI Roadmap as a living document, and that regular updates for all fields of science are necessary so that remaining RI gaps can be prioritised and solutions proposed.

BMS TWG held regular meetings with the coordinators of the 10 BMS RIs on the Roadmap to exchange best practice, to identify and discuss issues encountered by each RI initiative, and to work on identified bottlenecks which occurred on the way to implementation. The BMS RIs have worked together to create a common BMS RI Strategy in order to address the relevant policy stakeholders in Brussels and in each Member State to ensure long-term sustainability and the future of BMS RIs.

All BMS RIs on the current Roadmap show real promise towards implementation; some will apply for an ERIC while others will follow different legal organisational forms. The BMS RIs recognise their importance in providing the framework that will help Europe overcome the global Grand Challenges and to this end have integrated activities to ensure implementation is achieved. BMS TWG has monitored the intense cooperation between the BMS RIs and present in the BMS Report 2010, for the first time, a comprehensive overview of the links between all 10 BMS RIs and with other TWGs.

Members from across 30 different Member States have worked intensively to create the BMS Report 2010, which gives a clear and detailed insight into BMS **ERIL**. As outlined in BMS Report 2008, they would have welcomed more time for their deliberations. Further, the BMS TWG would have appreciated a better recognition of the Lessons Learned of the BMS Report 2008. BMS TWG again this time presents some recommendations for the successful future of the ESFRI process.

The Chair wishes to thank all independent external experts who worked in the three Expert Groups that evaluated the new BMS proposals. It is important to stress that the work of BMS TWG would not have been possible without the spirit and dedication of all members of BMS TWG

coming from so many different Member States and Associated States. BMS TWG members formed a big BMS family which is built on trust and friendship.

The Chair also wishes to express his gratitude to the BMS secretariat, Ingrid Zwoch, Dr. Silke Gundel and Marie-Christine Mahlke, who paved the way for BMS TWG in the update process and who worked tirelessly to make this BMS Report 2010 a reality. Very special thanks must go to the German Federal Ministry for Education and Research, who generously funded the BMS secretariat for more than four years.

The BMS TWG recommends three new RIs to ESFRI Forum for inclusion into the update of the ESFRI Roadmap 2010. Each of the RIs in this BMS Report 2010 addresses a real and specific need of European Life Sciences researchers for improved and more sustainable RIs, and also for future funding mechanisms to enable European researchers participate in the world league of Life Sciences research. ESFRI and its various editions of the Roadmap have strengthened competitiveness and progress toward reaching the Lisbon targets.

BMS TWG hopes that the BMS Report 2010 endorses **ERIL** and emphasises the importance of Life Sciences research in Europe. Life Sciences research deserves greater support and recognition for its role in generating a European-wide knowledge economy, generating innovation and growth, identifying solutions to tackle the Grand Challenges faced by Europe and the world, and improving and maintaining the health and well-being of European citizens for the benefit of mankind.



Chair of the  
Biological and Medical Sciences  
Thematic Working Group in ESFRI

# CONTENTS

<b>1. EXECUTIVE SUMMARY .....</b>	<b>1</b>
<b>2. BMS RIs AS A CONSTITUENT PILLAR OF THE EUROPEAN RESEARCH AREA ...</b>	<b>7</b>
2.1 European RIs in the BMS field .....	7
2.1.1 History of European RIs in the BMS field .....	7
2.1.2 Novel concepts for European BMS RIs .....	9
2.1.3 European added value of RIs in the Life Sciences area .....	10
2.1.4 Increased relevance of RIs in the Life Sciences area .....	12
2.1.5 Interrelation between the ESFRI and various national Roadmaps .....	14
2.1.6 Global dimension of the Life Sciences RIs .....	15
2.2 BMS Thematic Working Group's scope .....	15
<b>3. THE EUROPEAN RESEARCH INFRASTRUCTURE LANDSCAPE (ERIL) IN BMS ...</b>	<b>17</b>
3.1 ESFRI BMS Scientific Landscape .....	17
3.1.1 Cross-Cutting RIs and Biological Sciences .....	18
• Bioinformatics .....	18
• Bioimaging .....	19
• Structural Biology .....	21
• Chemical Biology .....	22
• Systems Biology .....	23
• Synthetic Biology .....	25
3.1.2 Biological Resources and Production Systems .....	26
• Biological Resources – genetic and biological resources .....	26
• Animals – production, health, welfare and livestock management .....	28
• Marine Biology .....	28
• Microbiological resources and production .....	29
• Plants – genetic and biological resources .....	29
• Analysis of ecosystems for agricultural research .....	30
• Impact of climate change on production systems .....	31
• Biological energy production .....	32
• Food and feed .....	32
3.1.3 Medical Sciences .....	33
• Biobanking .....	34
• Clinical Research .....	35
• Translational Medicine/Research .....	35
• Disease Models .....	37
• High Security Laboratories .....	37
• Biomedical engineering and related areas .....	38
3.1.4 Future Perspectives .....	39
• Towards the successful development of a European-wide integrated knowledge economy .....	39
• Access .....	40
• Data storage and management .....	40
• Impact .....	41
• Financial framework for construction and sustainability .....	42

•	Integration of Central and Eastern European Countries in the ERIL ....	43
•	Engaging with the global research platform .....	44
•	Emerging BMS fields and future challenges in biotechnology .....	44
•	Integrating efforts .....	46
3.2	Identified needs for a new generation of Life Sciences RIs .....	47
3.2.1	Systems Biology .....	47
3.2.2	Biorepositories – Microorganisms .....	48
3.2.3	Green Biotechnology & Biological Sciences .....	49
3.3	Processes beyond ESFRI .....	50
3.3.1	Survey on Research Infrastructures in the area of agri-food research .....	50
3.3.2	ERA-Instruments – an ERA-Net initiative for promoting infrastructure funding in the Life Science .....	51
3.3.3	ESF's/EMRC's strategy for medical Research Infrastructures in Europe ...	52
3.3.4	European Commission .....	53
<b>4</b>	<b>PROGRESS OF BMS RIs .....</b>	<b>57</b>
4.1	Introduction .....	57
4.2	The 6 first generation BMS RIs .....	57
4.3	The 4 second generation BMS RIs .....	58
4.4	Promoting synergies .....	58
4.5	Descriptions of the 6 first generation BMS RIs .....	59
4.5.1	Biobanking and Biomolecular Resources Research Infrastructure (BBMRI) .....	59
4.5.2	European Advanced Translational Research Infrastructure in Medicine (EATRIS) .....	73
4.5.3	European Clinical Research Infrastructures Network (ECRIN) .....	85
4.5.4	European Life Science Infrastructure for Biological Information (ELIXIR) ...	95
4.5.5	European Infrastructure for phenotyping and archiving of model mammalian genomes (INFRAFRONTIER) .....	107
4.5.6	Integrated Structural Biology Infrastructure (INSTRUCT) .....	117
4.6	Descriptions of the 4 second generation BMS RIs .....	129
4.6.1	European Marine Biological Resource Centre (EMBRC) .....	129
4.6.2	European Research Infrastructure on Highly Pathogenic Agents (ERINHA) .....	139
4.6.3	European Infrastructure of Open Screening Platforms for Chemical Biology (EU-OPENSOURCE) .....	151
4.6.4	Research Infrastructure for Imaging Technologies in Biological and Biomedical Sciences (Euro-Biolmaging).....	165
4.7	Contribution of RIs to different science fields .....	175
4.8	Common activities of BMS RIs .....	176
4.9	Conclusions .....	177

<b>5</b>	<b>EVALUATION OF NEW PROPOSALS .....</b>	<b>179</b>
5.1	Evaluation Procedure .....	179
5.1.1	Procedural guidelines for BMS Expert Groups .....	180
5.1.2	Modus operandi .....	181
5.1.3	Evaluation Criteria .....	182
5.2	Evaluation Results .....	183
5.2.1	Mature Proposals .....	183
5.2.2	Immature Proposals .....	186
5.3	Mature Proposal Templates .....	189
<b>6</b>	<b>LESSONS LEARNED .....</b>	<b>217</b>
6.1	Recommendations for the BMS sector .....	217
6.2	Recommendations for ESFRI .....	217
	<b>GLOSSARY .....</b>	<b>219</b>
 <b>APPENDICES</b>		
APPENDIX A:	LIST OF THE BMS TWG MEMBERS .....	227
APPENDIX B:	SUMMARY OF THE BMS TWG MEETINGS .....	233
APPENDIX C:	MEETINGS AND EVENTS OF THE BMS RIs .....	235
APPENDIX D:	LIST OF PROPOSALS ALREADY ON THE ESFRI ROADMAP .....	239
APPENDIX E:	LIST OF PROPOSALS RECEIVED AND ASSESSED .....	241
APPENDIX F:	LIST OF BMS EXPERTS .....	242
APPENDIX G:	LITERATURE .....	243





# 1 EXECUTIVE SUMMARY

Research Infrastructures (RIs) are one of the main pillars in structuring and integrating the European Research Area (ERA). They are the most powerful means to foster cooperation on a pan-European scale and to provide the required access to innovative methods and technologies for the advancement of science. Scientific progress, products, processes and services developed from it are key drivers of innovation and economic development and create with a growing mobility and improved training of the respective actors the basis for a strengthened European position (see Chapter 2 “BMS RIs as a constituent pillar of the European Research Area”).

Europe is facing major societal challenges (tightening supplies of energy, water and food, ageing population, ballooning public health expenditures and the risk of pandemics). As these Grand Challenges are strongly influenced by climate change and an increasing global competition, there is a continuous and even increasing demand to support a coherent and strategy-led approach to policy making on new and existing pan-European and global Research Infrastructures.

In 2002 the Competitiveness Council set up ESFRI (European Strategy Forum on Research Infrastructures) to meet this demand. Its Biological and Medical Sciences Thematic Working Group (BMS TWG), established in 2004 within the frame of the ESFRI Roadmap process, is now providing its third Biological and Medical Sciences (BMS) Report.

According to the mandate of the Thematic Working Groups, the BMS TWG identifies the needs for the installation of new RIs or the major upgrade of existing ones within its thematic scope. Due consideration was given to the respective research landscape, the rapidly changing structures thereof and its emerging and growing needs for networking and cooperation well beyond European borders (see Chapter 3 “Update of the Scientific Landscape”).

Terms of Reference – Thematic Working Groups,  
12<sup>th</sup> June, 2009

## Mandate of Thematic Working Groups

The following are the main activities that shall be undertaken by the TWGs:

- Monitoring of the scientific development and the need for RIs in the thematic areas, in consultation with existing relevant scientific organisations
- Following the implementation of the projects on the ESFRI Roadmap and giving expert feedback to ESFRI, e.g. on the needed coordination between different projects in the area
- Advising ESFRI on whether projects should remain on future editions of the Roadmap, and following a decision by ESFRI, to evaluate possible proposals according to the agreed procedure for the update of the Roadmap
- Advising ESFRI on potential improvement in the pan-European availability and management of existing RIs
- Coordinate interdisciplinary activities with the other TWGs

## Annex 1 to the Terms of Reference for Thematic Working Groups:

BMS TWG shall give attention to a stronger integration and closer cooperation between BMS initiatives included in the ESFRI roadmap and its updates.

BMS TWG can also evaluate proposals received by ESFRI according to the agreed procedure for the update of the roadmap.

To reflect the BMS research and funding scenery comprehensively, the report contains for the first time the views of other stakeholders and policy decision makers like the Standing Committee on Agricultural Research (SCAR), European Science Foundation (ESF), ERA-Instruments and the European Commission (see Chapter 3.3 “Processes beyond ESFRI”). Against this background the evaluation of new initiatives for RIs in BMS and the assessment of existing BMS RIs created the basis for the BMS TWG recommendations to the ESFRI Forum for the update of the ESFRI Roadmap 2010.

## Recommendations of the BMS TWG to ESFRI Forum

### RI proposals for the update of the Roadmap

The ESFRI stage-gate-process was started in March 2009 with the decision of the ESFRI Forum to launch a targeted call for RI proposals both in the fields of Energy and BMS. The BMS TWG received 9 proposals by the Executive Board of ESFRI. The evaluation procedure was executed during spring and summer 2010 with the support of external independent high-level experts. Based on individual assessments 3 Expert Groups ("Systems Biology", "Biorepositories – Microorganisms", and "Green Biotechnology & Biological Sciences") met for a consensus discussion and agreed on their recommendations to the BMS TWG with regard to the maturity of the proposals. Their views were guided by the needs of the potential user communities within the next 10 to 20 years (see Chapter 3.2 "Identified

needs for a new generation of Life Sciences RIs"). The strength of the scientific case and the extent to which the proposed RIs are technologically and financially feasible was taken into account as well as the possibility of open access for the user, the mechanisms for other partners to join in a later stage and to ensure the continuous upgrade of the RI in an open and effective way. Where appropriate, the work of the Expert Groups was supported by the input from another ESFRI Thematic Working Group (ENV TWG).

The Expert Groups recommended 3 proposals as mature for inclusion in the next edition of the ESFRI Roadmap. The BMS TWG unanimously accepted the recommendations in its meeting in June 2010. Hence, the BMS TWG strongly asks the ESFRI Forum to accept the 3 proposals for an inclusion into the Roadmap 2010 (see Table 1 and Chapter 5 "Evaluation of new proposals").

**Table 1:** 3 BMS RIs recommended by BMS TWG to be included in the ESFRI Roadmap 2010

<b>ISBE</b>	Infrastructure for Systems Biology – Europe
<b>MIRRI</b>	Microbial Resource Research Infrastructure
<b>ANAE</b>	Infrastructure for Analysis and Experimentation on Ecosystems

### The 10 BMS RIs of the Roadmap editions 2006 and 2008

The continuous monitoring of the preparation and implementation phases of the BMS RIs of the past Roadmaps (2006 and 2008) facilitated assessment of their progress and contribution to their respective evolving scientific fields. The 10 BMS RI projects are listed in Table 2.

In line with the mandate to support ESFRI in its incubator role, BMS TWG organised regular meetings with the coordinators of the 10 BMS RI initiatives. Important updates on national roadmaps and decision making processes, the implementation of a new European legal status for Research Infrastructure Consortia (ERIC) as well as intense supporting activities helped in paving their way towards realisation.

There was an intense exchange of best practise between the 6 "First Generation" RIs (BBMRI, EATRIS, ECRIN, ELIXIR, INFRAFRONTIER, INSTRUX) of the 2006 ed. of the Roadmap and the 4 "Second Generation" RIs (EMBRC, Euro-Biomed, ERINHA, EU-OPENSOURCE) of the 2008 Roadmap.

The 10 BMS RIs, which all have received or will receive EU funding for the Preparatory Phase (PP), during which infrastructure construction and operation plans will be developed, have joined forces in order to work towards a more political and sustainable funding support for their future implementation. To that end, the group has produced a Strategy Paper in which it outlines the role and importance of BMS RIs in addressing the future challenges Europe faces (see Chapter 4.8 "Common activities of BMS RIs").

Progress, developments, collaborative efforts and Member States commitments for each of the 10 BMS RIs are detailed in Chapter 4 (see Table 2 and Chapter 4 “Progress of BMS RIs”). BMS TWG concludes, following careful consideration of each BMS RI initiative, that all are making

sufficient and promising progress through their respective stages of the ESFRI process. BMS TWG advises ESFRI that all 10 BMS RIs should remain on the ESFRI Roadmap and proceed to Construction Phase.

**Table 2:** Of 10 BMS RIs, six were included in the ESFRI Roadmap 2006 and received EC funding for their Preparatory Phases, which ends for those initiatives during 2010/2011 (highlighted in dark orange). Four RI initiatives added to the updated Roadmap in 2008 will receive EC funding for the Preparatory Phase in 2010/11 (highlighted in light orange).

<b>BBMRI</b>	Biobanking and Biomolecular Resources Research Infrastructure
<b>EATRIS</b>	European Advanced Translational Research Infrastructure in Medicine
<b>ECRIN</b>	European Clinical Research Infrastructures Network
<b>ELIXIR</b>	European Life Science Infrastructure for Biological Information
<b>EMBRC</b>	European Marine Biological Resource Centre
<b>EU-OPENSREEN</b>	European Infrastructure of Open Screening Platforms for Chemical Biology
<b>Euro-Biolmaging</b>	European Biomedical Imaging Infrastructure
<b>ERINHA</b>	European Research Infrastructure on Highly Pathogenic Agents
<b>INFRAFRONTIER</b>	European Infrastructure for Phenotyping and Archiving of Model Mammalian Genomes
<b>INSTRUCT</b>	Integrated Structural Biology Infrastructure for Europe

### Challenges and perspectives of the BMS RI landscape

The raising awareness towards major societal challenges has strongly influenced policy decisions such as the Lisbon treaty, the EU Vision 2020 and the European Research Area. Europe is striving for adequate governance and funding concepts to cope with the increasing demand on research, technological development and innovation required to meet its objectives for a sustainable welfare of its citizens and a resource-efficient economic growth.

Requirements coming along with the demographic change are of growing importance for the self-concept of European citizens, their welfare, inclusion and participation in decision making processes, and their life-course. Besides prevention, diagnosis and therapies of diseases extended attention has to be paid to the citizens' mobility, independence and access to information and services. Cooperation between disciplines, research and

innovation actors, private and public sectors as well as users of services and support (e.g. care and rehabilitation) will become more essential than ever. The same applies for the continuous growing use and exploitation of biological resources, both for food or non-food applications. Protection of consumers, the environment and the diversity of organisms have to be considered in view of a growing demand for energy production.

Multidimensional RIs in the BMS sector are playing a key role in addressing the major societal challenges Europe is facing. Whether they are of a horizontal nature supporting a variety of disciplines with their services or of a vertical nature covering the value chain in a specific scientific sector, their complementary nature provides for unprecedented opportunities in a wide range of research topics and technological development questions if adequately structured and networked. To fully benefit from their scientific, technological and innovation potential, the following major

efforts for a coherent strategy are required on a European, national and regional level:

- Embedding the RIs strategically in a well-funded research and development environment, which will increase mutual exchange of excellence and expertise and allow for the flexibility required by the continuously changing demands and at the same time secure the organisational and financial framework for their reliable planning and implementation,
- Enhancing integration of the newly developing RI activities with existing ones; this will bridge existing gaps and prevent unnecessary overlaps in activities without losing the benefit of mutual stimulation in progressing towards innovative methods, technologies and trans-disciplinary scientific fields,
- Improving the involvement of a variety of user communities from the public and private sector; this will strengthen existing and stimulate emerging outreach functions to currently poorly harnessed regions, improve and adjust services according to the user demands, and contribute to the economic development of the different RI sites,
- Safeguarding the distribution of know-how, knowledge and skills as well as resources, methods and technologies,
- Strengthening the research and innovation activities with a coherent strategy of career development, such as providing training for skills and know-how in science, innovation, administration and management, and policies,
- Increasing the visibility of research and innovation capabilities and capacities beyond European borders to attract world-wide excellence and strengthen global cooperation, and
- Supporting and enlarging harmonisation and standardisation efforts to ensure and increase the

quality of services provided and to initiate comparable developments on local and regional levels.

On the basis of its scope the BMS TWG described a scientific landscape of RIs in the Life Sciences, incorporating the RIs already on the Roadmap, RIs which are suggested to be taken onboard in the 2010 update and future RI needs that are still to be addressed (see Chapter 3 “The European Research Infrastructure Landscape (ERIL) in BMS”). Within its scientific field BMS TWG thereby drafts the concept for a **European Research Infrastructure Landscape (ERIL)** to successfully reach the European Research Area.

Lessons learned from the recent update of the BMS Report show a need for a more targeted approach in identifying new and emerging fields. Following an in-depth analysis of the 3 thematic pillars of the BMS TWG’s scope – “Biological Sciences”, “Biological Resources and Production Systems” and “Medical Sciences” - emerging and fast developing fields could be identified. ESFRI should in future take into consideration the infrastructural needs of areas like synthetic biology, bioenergy and agricultural research (see Chapter 3.1.4 “Future Perspectives”).

A continuously updated pan-European inventory survey created by and/or combined with information available on national and regional level would help to speed up responses to the specific needs and to meet the demands more efficient and effectively (see Chapter 6 “Lessons Learned”). Foresight activities could contribute tremendously to fields and disciplines not yet covered.

A permanent system for monitoring and assessing the impact of the BMS RIs would facilitate EU-wide, regional and national decision making processes. A coherent set of criteria should be developed, and these should reflect the similarities and differences of the BMS RIs by taking into account their objectives, specific structures and operation modalities. The impact of the BMS RIs on the knowledge triangle – research, training and innovation – in boosting innovation and economic developments should be judged and factored in relevant policy decisions.

The development of adequate access schemes requires comprehensive attention with regard to the specifics of each BMS RI, balancing the need for openness and transparency with the interests of the institutions who in a flexible geometry are responsible for establishing, operating and using them.

The recently created legal framework, ERIC, is a promising support for setting up and operating pan-European Research Infrastructures. First application attempts on-going are closely monitored by those RIs where the decision on the legal frame is still pending. An intense and continuous exchange of experiences will help to facilitate future applications.

In future ESFRI and its TWGs need to play a much more proactive role in achieving the optimum benefit for European Research. Both ESFRI as well as the TWGs need sustainability, which only can be reached by institutionalisation of ESFRI (legal personality and budget). Since the RI landscape is rapidly changing and expanding in face of the Grand Challenges, the Roadmap has to be an open, regularly up-dated living document (see Chapter 6 “Lessons Learned”).

Europe has to provide answers to the Grand Challenges rather than set limits as to how many RIs are on the ESFRI Roadmap.

Summarising the discussions and considerations within the Thematic Working Group Biological and Medical Sciences during the update process, we propose that the role of ESFRI should be reinforced with regard to the governance of European research and innovation programming and funding. A coordinated approach to link its activities with those of the major committees responsible for the implementation of European programmes like ERAC (European Research Area Committee), the former CREST (Comité de la recherche scientifique et technique) and the Programme Management Committees for the Framework Programme of the European Union would be instrumental for the constitution and design of a coherent and successful **European Research Area**, an ERA which finds its sound basis in a well established **European Research Infrastructures Landscape (ERIL)**.



## 2 BMS RIs AS A CONSTITUENT PILLAR OF THE EUROPEAN RESEARCH AREA

### 2.1 European RIs in the BMS field

Biological and Medical Sciences Research Infrastructures (BMS RIs) are addressing a wide range of research and technological development questions related to humans, animals, plants and microorganisms on all organisational levels like organs, tissues, cells and sub-cellular structures with different physical, chemical and biological properties – their interaction with and influence of biotic and abiotic factors and the changes related to their respective environment, development and behaviour.

Key technologies and know-how for the creation and processing of data, the modelling of processes and interactions as well as for the monitoring of developments and relationships between research objects are trans-disciplinary in nature. They are required for the fundamental understanding of different interactions and processes and the key factors controlling them. Their applications in various societal fields generate a sustainable influence on policy areas like health, consumer protection, environment, agriculture, fisheries and are contributing to the economic development.

Existing BMS RIs with their growing variety in themes, methods and techniques are not only representing the heterogeneity of the Life Sciences sector but reflect the history of research and innovation funding at their structural and institutional levels.

BMS RIs share a number of common features:

- They are distributed rather than single-sited, rarely virtual,
- They consist of heterogeneous institutional organisation and funding,
- They overlap with other scientific fields i.e. environment/climate/earth systems, energy, information and communication technologies, material sciences, social sciences and humanities,

- Vertically oriented RIs focus on a theme/a well defined set of research objects; horizontally oriented RIs focus on key technologies as services for a broad range of disciplines i.e. biotechnology and modelling,
- The commercialisation of services within RIs is, in principle, possible and there is a great variety of developmental stages in this respect.

#### 2.1.1 History of European RIs in the BMS field

As most of the RIs in the BMS field developed in direct association with the respective research and user community, their building up to international and European organisations needed quite some efforts to achieve a common understanding of research and innovation concepts and approaches.

Success of BMS RIs relied on the understanding, that the integration of excellent basic research, the provision of services to the scientific community, and the training of scientists are underlying a continuous process. This is a process which contributes to the timely and unique availability of know-how and technologies for the society at large.

EMBL, the European Molecular Biology Laboratory, founded in 1974, is Europe's flagship infrastructure supported by public funding from 20 Member States and one Associated Member. Research organised by a main centre and several outstations is currently conducted by approximately 85 independent groups covering a broad range of research areas in cellular and structural biology, and bioinformatics. EMBL can be regarded as an outstanding example of RI developments in the BMS area.

RIs established in parallel or subsequently in Europe – like the Institute Laue-Langevin in Grenoble (ILL), Conseil Européen pour la Recherche Nucléaire, (European Council for

Nuclear Research, CERN), European Organisation for Research and Treatment of Cancer (EORTC) or European Culture Collections' Organisation (ECCO) followed the same pattern combining world-class research and services. All BMS RIs, either large medium-sized or small RIs, have benefited from:

- A critical mass of the required technologies and equipment combined with the necessary support for maintenance and adaptation,
- The establishment of development settings where technologies and instrumentations may be taken up and combined as they arise pushing them forward into new fields,
- The creation of an inspiring research environment of different disciplines strengthened by a mutual exchange with leading laboratories within and well beyond European borders,
- Close cooperation with and between sectors making use of the existing knowledge in technology transfer and marketing of products, processes and services,
- Intensive networking with RIs outside the biology field, ranging from the sharing of data and results to the establishment of partnerships for the mutual use of technologies and equipment or the exchange of staff,
- A reliable system to select and decide on research and innovation priorities,
- Careful selection of promising young researches and research group leaders properly equipped and funded with a high degree of independence for pursuing own research aims and objectives,
- A wide range of opportunities for career development,
- Balancing the exchange of expertise and experiences through pan-European mobility of researchers and technicians with a sufficient continuity of own research and

technological development activities ensured by internal research programmes and agendas,

- Providing internal and external training schemes which allow for the dissemination of scientific approaches and achievements as simultaneously for the aggregation of expertise and excellence.

The complexity of the **BMS field** creates challenges for research and innovation activities which strongly depend on cooperation in a European and international scale. It is – with a growing cohesion of existing facilities and the structured extension and integration of new and emerging resources – going well beyond those research objectives which are trans-national by nature.

Providing **access to external users** puts a strong demand on the organisational features of the BMS RIs. Extended access schemes resulted in a growing network contributing to the competitiveness of the research community via the continuous adaptation processes for the needs of the respective user communities. Especially the user-orientation strengthened the service components of the BMS RIs concerned. Consequently the awareness for intellectual property aspects was raised. **Innovation activities** ranging from the protection of knowledge and know-how, its use and exploitation for applications and research became an integral part of the RI activities and promoted the transfer of technologies, procedures, processes and services by a wide set of targeted dissemination schemes thereby extending the skills of the actors involved.

**Standardisation and harmonisation schemes** are – at the same time – the result and the source of trends useful to strengthen the competitiveness of research and innovation. In the BMS area their application in RIs does not only safeguard the quality of research and technological developments but in many cases they create the research basis in the first place.

Of major importance are standard operating procedures (SOP) to collect, store and handle data of basic and applied research,



i.e. data for modelling, clinical data, to preserve them, particularly if it concerns personal data, and to harmonise procedures for the collection, storage and handling of materials of different biological origin (human, animal, plant and microorganisms).

The usefulness of standardised and harmonised approaches is most obvious where **ethical matters** are concerned. Based on fundamental regulations on national and international level, their improvement and implementation in the BMS area has been continuously watched and reported. Ethical aspects of utmost importance for the Life Sciences sector are related to informed consent, i.e. children, people not able to give consent, adult healthy volunteers, human genetic material or biological samples, human data collections; research on human embryos and foetus, i.e. tissues/cells, stem cells; privacy, i.e. genetic information or personal data, i.e. health, sexual lifestyle, ethnicity, political opinion, religious or philosophical conviction; research on animals; research involving Developing Countries and dual use. Those quality standards have an outreach function not to be underestimated for the future integration of upcoming or currently isolated resources.

The development of an attractive, open and sustainable European labour market for researchers was the major aim of the European Charter for Researchers. The proposed framework conditions allow for recruiting and retaining high quality researchers in environments conducive to effective performance and productivity. Hence, the institutions involved in BMS RIs strived to apply administrative and legal regulations to improve trans-national training and mobility targeted at researchers, technicians and research and innovation managers. The BMS area was due to the typical multi-sited organisation of its RIs deeply involved to overcome the obstacles identified by the Charter, i.e. the portability of both grants and social security provisions, in accordance with national legislation.

According to the mostly distributed nature of the BMS RIs the building-up to pan-European partnerships or even institutions was characterised by the **involvement of actors from different organisations**

**(public or private) and sectors (scientific, political, economic).** Legal and governance aspects had to be negotiated and agreed on taking the varying objectives and interests into due consideration. The structures of the BMS RIs differ considerably among each other and reflect their respective nature. Some of them are of a vertical nature focussing on a research area/theme; others are of a rather horizontal nature, delivering services to a broad range of disciplines. Therefore there was no uniform scheme available for the institutionalisation of the BMS initiatives. Comparable difficulties were to solve with regard to the financing of the BMS RIs. Framework conditions vary considerably between funding organisations – and are dependent on the regulations applicable for extra-/intra- mural funding or type of costs occurring. National and regional regulations scrutinised for applicable procedures and decision making needed practice validation.

During the last decades national efforts to foster and structure the BMS RI field were complemented by the European Framework Programme for Research and Technological development (FP). The predominantly bottom-up organised process on EU level to support the design of new RIs, the preparation of new or major upgrades of existing RIs, and their subsequent networking and integration pushed the RIs towards excellence, enhanced their visibility beyond Europe and contributed tremendously to their competitiveness. However, in a steadily growing, yet fragmented, European Union the development of the BMS RIs has raised awareness of national and international decision makers that their research funding policies should focus on RI developments in challenging fields and, at the same time, set up and encourage RI initiatives in emerging areas.

### 2.1.2 Novel concepts for European BMS RIs

Recent developments in the BMS field have shown that the thematic, methodological and technical framework of RIs is crucial for the required flexibility in an expanding research field. Adaptation according to the dynamics of the research areas concerned is requiring the reliable and successful

integration of new developments into the existing structures. New and upcoming developments have to be observed and accompanied in a strategic and coherent approach against the background of the evolving RIs concerned and the whole developing BMS RI landscape.

ESFRI's Thematic Working Group in the Biological and Medical Sciences is the central mechanism for a timely, strategically, and jointly organised identification of RI demands in its scientific remit – whether for new or the upgrade of already existing RIs. The actors and institutions involved have an extended mandate to act as supporters for RI initiatives and recommend to the ESFRI Forum all measures regarded as useful for a coherent development.

In addition to the coordination activities implemented by the BMS TWG, the group aims to position research actors and innovation performers with adequate funding mechanisms. Regular meetings with the Representative of the European Commission for the Framework Programme (Specific Programme Capacities) facilitate the exchange of information and advice on opportunities.

The design and preparatory phases for RIs, which are funded by the European Commission, allow to examine their feasibility and to validate the scientific and financial concept before national investments are decided. Continuity is granted by the top-down-organised support from the EU for the integration of RIs. The competition between RI initiatives and the peer-reviewed selection ensures excellence and quality. The recent change in the EU funding paradigm of preparatory awards and integrating measures – from bottom-up organised to top-down – steers the RI process towards a less fragmented landscape.

Depending on the nature of the BMS RIs – horizontal or vertical – costs for running, maintaining and continuous development of a BMS RI may exceed those for the initial installation. BMS RIs would extremely benefit from an extended user community and improved access schemes. However, the financial pressure thereby exerted on the running and maintaining of the

respective RIs should be considered simultaneously. Political decision makers will soon be confronted with the need to adjust the concept of existing funding opportunities.

Monitoring the developments of RIs in the BMS area will become an equally important component of the BMS TWG role as foresight activities to identify future needs for BMS RIs. Both create the basis for the prioritisation of pan-European RIs. The cooperation of the ESFRI BMS TWG with relevant institutions (European Commission, ESF) and committees like SCAR or ERA-Nets helps together with the support of the coordinators of RI initiatives to detail the picture of the BMS landscape (see Chapter 3.3 “Processes beyond ESFRI”). A periodic inventory survey as recommended by ERAB, the European Research Advisory Board is still under discussion.

Productivity and efficiency of the mostly distributed organised Research Infrastructures in the Life Sciences area strongly depend on careful analyses and assessments of the location (sites) and their potential – based on a reliable set of criteria for this selections procedure and the establishment of approved procedures. The socio-economic impact of BMS RI sites has yet to be fully explored and developed.

### 2.1.3 European added value of RIs in the Life Sciences area

The chapter “Research Infrastructures and their role in strengthening research capacity within the ERA” is headed by the following paragraph:

*“Research Capacity must be interpreted within the context of research requirements. It describes the potential that arises via the combination of scientific knowledge, technological expertise, managerial skills and other human and physical resources to address specific research questions. Within the ERA it refers to the need to combine these elements in ways which facilitate collaborative efforts by all Member States to promote effective, efficient and ground-breaking research.”<sup>1</sup>*

<sup>1</sup> Report of the Expert Group on Research Infrastructures, European Commission, 2010

This is downright appropriate for Research Infrastructures in the Biological and Medical Sciences area.

The combination and integration of already existing and newly developing RI services and resources helps to foster and strengthen the scientific and technological capacities required well beyond the means of single states and beyond research fields.

The combination of recent and future national BMS RI investments creates an unprecedented critical mass of scientific, technical and managerial expertise and excellence. A critical mass, which improves the flexibility to react on the continuously changing research and development demands in the research areas covered. Adaptations can be realised jointly and efficiently making best use of combined and/or specialised research and innovation offers, thereby increasing the visibility of the R&D fields as well as its actors in the different countries.

The complementary nature of BMS RIs, especially with regard to disciplines involved and services provided, is a major force to overcome the still existing fragmentation and to focus disparate approaches without losing the benefit of mutual stimulation attended by it for new and innovative conceptions. In contrary, BMS RIs are – as an integral part of national institutional and project funding strategies of different states – transmittance platforms of research and innovation trends in themselves - between and within states.

Objects, objectives, fields and disciplines, scope, scales and ranges of BMS RIs are extremely complex. Their dimensions – roughly outlined below – create an enormous leverage effect for their single nodes and sites, if properly structured, networked and integrated:

- Molecules – cells – tissues – organs – organisms – biotopes – ecosystems - biospheres
- Microorganisms – plants – animals – humans (incl. model organisms/indicator organisms for specific research questions)

- Prevention – detection – diagnosis – monitoring – prediction
- Basic research (creation of knowledge and data) – applied research in different fields – clinical research – technological development – validation and demonstration – innovation and implementation activities – manufacturing and engineering – modelling – policy support – management
- Theoretical – interventional (e.g. therapeutic, mitigation) – and experimental approaches – assessment (e.g. life-cycle, quality, risk)
- Influences of biotic and abiotic factors and their interrelationships
- Dynamics and interdependencies in space, time and developmental stage
- Structural and/or functional relationships
- Biology, biotechnology, medicine, agriculture, forestry, marine sciences, physics, mathematics, computer sciences, chemistry, geology, social sciences and humanities, ecology, environmental sciences incl. meteorology, geology, and engineering

National investments can be maximised by continuous pan-European mobilisation, sharing and exchange of knowledge, know-how and data in strengthening the potential with regard to each of the dimensions mentioned above. Remarkable added values are:

- Advancements can be accelerated, if not enabled at all,
- Achievement in the minimisation of overlaps where they are regarded as inappropriate,
- Identification and bridging of existing gaps,
- Expanding into emerging or so far not-accessible research and innovation fields,
- Intensive stimulation and evidence-based validation of approaches and results as well as their subsequent

transformation into products processes and services,

- Overcoming cultural boundaries – between disciplines, sectors and institutions – by taking up existing experiences and adapting them according to the specific needs of researchers, technicians, managers – and users,
- Harmonisation and standardisation as tools and mechanisms for sustainable and increasing quality, safety and security.

Trans-national cooperation can as well be beneficial for the efficient use of national resources where mutual specialisation is organised at an equitable level and is jointly organised in a complementary and structured RI. National investment can focus on specialised services instead of offering all costly services at all sites.

A key element for these European added values is a fair, transparent and appropriate access to data, results, knowledge, methods and technologies and the commonly organised management and support structures. Essential is the brain circulation associated with it – on all organisational and structural levels – organised and implemented as an open staff recruiting policy, as simple exchange measures or joint training and career development programmes.

#### 2.1.4 Increased relevance of RIs in the Life Sciences area

The way Europe responds to the Grand Challenges will shape its future in the decades to come.

During the Swedish EU presidency 2009 Europe had agreed on a new and unprecedented concept of **Joint Programming** (JP) to address major societal challenges by making the most of national budgets allocated to research in a flexible and jointly organised geometrical approach.

*“These challenges include sustaining Europe's prosperity in the face of increased global competition; dealing with the needs of its ageing population and the challenges of*

*immigration; and stimulating sustainable development, especially in the context of climate change, securing the supply of energy, preserving human and environmental health, ensuring food quality and availability as well as safeguarding citizen security.”<sup>2</sup>*

First initiatives to tackle common challenges most efficiently have been already launched, some if not most of them within the Life Sciences area or at least strong Life Science components:

The Pilot Initiative on **Neurodegenerative Diseases**, in particular Alzheimer's disease, has the objective to pool the resources and better coordinate the research efforts of Member States in this field. There are currently over seven million people with Alzheimer's disease and related disorders in Europe and it is predicted that this number will double in the next 20 years. Therefore it is vital to plan, invest and cooperate in this field today both to control the social costs of these diseases as well as to offer hope, dignity and healthier lives to the millions of sufferers and their families.

The BMS RIs contribution is manifold, like cutting edge bioimaging tools combined with technologies, methods and (biobanked) materials derived from the “-omics” sector, disease models applicable in diagnostics, the design, delivery of therapeutic, even personalised interventions and/or monitoring progression of the disease, protective or even restorative answers to interventions; systems, synthetic and chemical biology approaches for drug design, delivery and a deepened understanding of the aetiology and course of the disease and possible adverse effects of interventions; translational and clinical research services – covering the range from the inception to its introduction to the consumer market and beyond – including the (pre)-clinical study phases and the required improvement of efficacy and safety of drugs, treatment, medication and intervention schemes.

<sup>2</sup> Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the regions towards Joint Programming in Research: Working together to tackle common challenges more effectively; Brussels, 15.7.2008, COM, (2008), 468 final

**Agriculture, Food Security and Climate Change** – the overarching objective of this Joint Programming Initiative (JPI) is to integrate adaptation, mitigation and food security in the agriculture, forestry and land use sector. Co-benefits in terms of reducing emissions and increasing resilience of farming, forestry and biodiversity to climate change are expected by jointly identified and promoted measures.

The development of a systemic understanding is the key knowledge objective of the Joint Programming Initiative. Hence, BMS RIs are predestined actors contributing to the integration of a large range of disciplines like climatology, ecology, biology, agronomy, forestry and socio-economy through plant, soil and animal sciences, that shall be strongly connected around a central spine of agro-ecological modelling.

Adapting planning in agriculture cannot only rely on knowledge about global climate patterns, but needs detailed information on regional impacts and meaningful assessment of the adaptive options and their feasibility at local and farm level to which the BMS RIs will adequately offer regional and/or local services supplied and supported by their capable networks and distributed sites. However, internationalisation is a strong demand – so close interaction with existing international research activities (e.g. Earth System Science Partnership, ESSP) and results such as The Economics of Ecosystems and Biodiversity (TEEB11) study as well as existing models for enhancing ecosystem functioning and services will be taken into account.

The second generation Joint Programming Initiatives are not yet as advanced as the ones of the first generation or the Pilot Initiative. However, outlines have been formulated by the proposing Member States showing the clear need for the integration of BMS Research Infrastructures into their programmatic approaches.

**Health, food and prevention of diet related diseases** will rely on the expertise and services of the health oriented BMS RIs but as well on those RIs related to the whole value chain of food production, processing,

packaging, manufacturing storage, transport – covering the varieties of food chains from the different sources, e.g. agriculture, aquaculture, fisheries, up to the consumers, their behaviour and protection. Underpinning the importance of health as a key driver for Europe's growth and prosperity, this JP Initiative has identified major challenges for putting cost effective interventions in place to improve health status and resulting in economic benefits for society and future productivity and competitiveness.

The initiative **Healthy and productive Seas and Oceans** has beyond its environment components a strong orientation towards Life Sciences in addressing the needs for a sustainable use of natural especially biological resources – for food and feed as well as non-food applications. The enormous biodiversity of these ecosystems could offer a variety of opportunities for novel products or sources for industrial applications, e.g. bio-processing, biomass, bioenergy, bio-materials, pharmaceuticals. Bioprospecting, exploitation and use will concern microorganisms, animals, plants – their physiological performance and genes and has a tremendous potential to draw from cooperation with BMS RIs.

**More years, better lives** – increased life expectancy and continuous birth rates below the replacement level have changed population age structure considerably and will influence character and self-concepts of society and its members, e.g. people's understanding of inclusion, participation, welfare, equality, and life course. The areas health & performance, work & productivity, welfare & social systems, education & learning, housing, urban-rural development & mobility, are the main areas deserving particular attention – and will need the support and services of BMS RIs in cooperation with the Social Sciences and Humanities (SSH) RIs. Contextual influences, individual behaviour, genetic disposition span the field for the Biological and Medical Sciences.

The Joint Programming Initiative **Antimicrobial resistance** addresses the following major dilemma: health care has come to depend on the use of drugs to combat infectious microorganisms, the more frequently they are used, the less effective

they will become in the long run. It stresses, that the need for antibiotic therapy in modern health care will remain high and is anticipated to increase even further with an aging population and increased global infection rates. The identification of new molecular markers, novel lead molecules for antibiotic treatment methods, of refined prescription of antibiotics and strategies for modelling of global epidemiology, risk assessment and disease burden of antimicrobial resistance requires comprehensive solutions with measures from many sectors of society, policy makers, health care, education, industry, environmental agencies, agriculture, veterinary medicine, research, and other areas and to which the BMS RIs can and will offer their expertise and their resources.

The JPI **Water challenges for the changing world** – is addressing a growing gap between global water demand and water supply, potentially intensified by a fast approaching biobased economy and the discharge of waste water to the environment. Our ecosystems will be threatened by overexploitation of water sources and increased pollution. This situation will be influenced by and tightened due to climate change, where drought in some areas and flooding in others will also damage the ecosystems and society as a whole. Although the focus of this JPI is research programming on water and hydrological issues, interfaces with BMS RIs are obvious: drinking water as part of our daily nutrition, pollution and infections and agriculture.

The second generation of JP Initiatives was adopted by the European Council on 26<sup>th</sup> March 2010 on the same common understanding as the first generation – voluntariness, openness and a variable geometry for the national decision makers. Together with the ESFRI Strategy 2020 and the pan-European Research Infrastructures initiatives they will provide major pillars of the European Research Area and fit well into the Vision 2020 of the EU – both directed towards smart, sustainable and inclusive growth with the main objective to improve the conditions for research and development and raise the combined public

and private investment levels in this sector to 3 % of the gross domestic product.<sup>3</sup>

### 2.1.5 Interrelation between the ESFRI and various national Roadmaps

European Member States have dedicated intensive efforts to the development of a joint roadmap for pan-European Research Infrastructures. In stirring these efforts ESFRI has initiated a major change in European research activities and its funding.

The BMS TWG benefited from previous roadmap experiences in and beyond Europe. It provided its first report in 2006 and submitted the updated report in 2008 to the ESFRI Forum. The present report of the BMS TWG reflects the evolving roadmapping process and the mandate of the group to foster the implementation of BMS RIs.

In executing their incubator role, the Working Group members, mostly national decision makers, have the responsibility to prepare and implement national decisions on pan-European RIs. Their structure, objectives and operability are discussed in the relevant national fora and are assessed with regard to the needs and demands of the scientific community. Guiding principles may vary between national programmes but correspond on fundamental criteria:

- The involvement of excellent researchers and institutions,
- Provisions and scope for outstanding research,
- The complementarity of programme approaches,
- The utilisation by several research groups with highly advanced research projects,
- Openness and easy access,
- Long-term planning addressing (i) scientific goals, (ii) financing, and (iii) its use and (iv) the socio-economic benefit for the national scene,
- Typically multi-sited, it is well recognized that the BMS RIs create

<sup>3</sup> European Council Conclusion of 16<sup>th</sup> June, 2010

opportunities even for those countries with limited funding capacities.

Regular meetings of the responsible ESFRI BMS delegates ensure an efficient update on national developments and allow for synchronisation of the mapping procedures. The ESFRI process has had a tremendous impact on promoting the planning of national roadmaps for RIs. This impact is particularly strong in fields, such as Life Sciences, which until now have not had a long tradition of joint planning and pooling together resources for large-scale RIs. Many European Member States have recently prepared or are in the process of preparing their own roadmaps, and the ESFRI RM is of high importance for that preparation. The ESFRI RM and the national roadmaps have a very positive feedback effect on each other, offering the prospect of a proper and efficient implementation of its RIs through a reliable and increasing level of sustainable financing.

The increasing awareness that the achievement of breakthroughs depends on advanced facilities and more comprehensive and accessible resources, has created a jointly executed responsibility for the competitiveness of Europe facing major societal challenges.

### 2.1.6 Global dimension of the Life Sciences RIs

As the Report of the Expert Group on Research Infrastructures indicates, *“the realisation of the European roadmap for the Research Infrastructures is of outmost importance within the process of the implementation of the 2020 Vision for the European Research Area (ERA) in view of the globalisation of research and the emergence of new scientific and technological powers China and India”*.<sup>4</sup>

The Expert Group points out that across all scientific disciplines, research activity increasingly involves international collaboration, either because of the need to pool knowledge and share RIs or through the very nature of the research challenges

being addressed. Global research challenges emanate from problems and issues that have a world-wide impact across nations as major scientific issues. They are of a scale or complexity that goes beyond the reach of most national resources and have to be addressed on the global level. Europe is regarded as well positioned to either take or to share leadership with other nations in addressing such challenges, or to provide the focus for relevant expertise and RIs within a global network.

This assessment is shared and supported by the G8 and G5 whose research ministers acknowledged the necessity of promoting international cooperation through the exchange of relevant information, providing access to RI facilities for public and private users and to promote the mutual international use of RIs by involving relevant actors in the design and planning phases for new RIs.

Global cooperation is a matter of course for all BMS RIs. The intensity and character of it is depending on the research and innovation field addressed. A number of BMS RIs show a global dimension right from their start (e.g. ELIXIR, INFRAFRONTIER, BBMRI, EMBRC). Others are continuously improving their global outreach, with regard to research and technical links. Some of them have already institutionalised their interactions (see Chapter 4 “Progress of BMS RIs” for detailed information on international participating members).

### 2.2 BMS Thematic Working Group's scope

In June 2009 ESFRI Forum decided that its Working Groups should be renamed in order to demonstrate that ESFRI's task is not only the updating of a Roadmap but strategically directed towards Europe's Research Infrastructure area as a whole. Therefore the mandates were broadened from Roadmap Working Groups to Thematic Working Groups.

The new mandate of the Thematic Working Groups is focussing on research landscapes, the identification of gaps or areas missing, the need for coordination and networking and in overviewing and supporting the projects on the roadmap to

<sup>4</sup> Report of the Expert Group on Research Infrastructures, European Commission, 2010

get off the ground (see Chapter 1 “Executive Summary”, Terms of Reference/Mandate of TWGs). BMS TWG’s exploration activities for new or the major upgrade of existing Research Infrastructure initiatives stayed within the scope of ESFRI’s limited call: the area of agri-food, systems biology and other related sectors.

The BMS TWG scope covers the whole range of the Life Sciences area – from basic biological sciences, biological resources and production systems through to medical sciences. Table 3 lists major sectors, but is by far not exhaustive. The rather horizontally oriented BMS RIs are offering services to the research and innovation community in the whole range, whereas the more vertically oriented are active within one or only few of the sectors given.

**Table 3:** Scope of the BMS Thematic Working Group

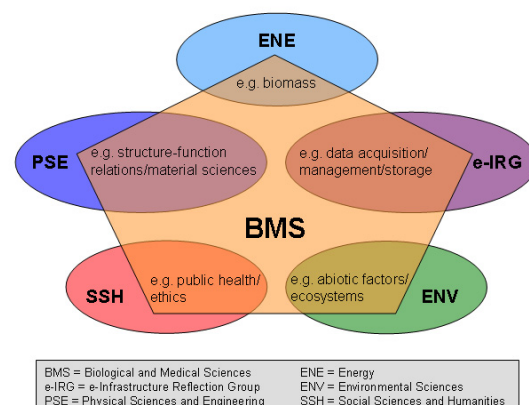
Biological Sciences		Biological Resources and Production Systems			Medical Sciences		
<ul style="list-style-type: none"><li>• Evolution</li><li>• Development &amp; diversity of organisms</li></ul>	<ul style="list-style-type: none"><li>• Anatomy &amp; physiology of organisms</li><li>• Behaviour &amp; ecology</li><li>• Interaction of organisms</li></ul>	<ul style="list-style-type: none"><li>• Plants</li><li>• Animals</li><li>• Micro-organisms</li><li>• Bioenergy &amp; biofuels</li></ul>	<ul style="list-style-type: none"><li>• Sustainability</li><li>• Safety and quality</li><li>• Health &amp; welfare</li><li>• Infectious diseases</li><li>• Zoonoses</li></ul>	<ul style="list-style-type: none"><li>• Human nutrition</li><li>• Aquaculture</li><li>• Agrifood</li><li>• Livestock production</li></ul>	<ul style="list-style-type: none"><li>• Epidemiology</li><li>• Aetiology research</li><li>• Biomedicine</li></ul>	<ul style="list-style-type: none"><li>• Prevention</li><li>• Diagnosis</li><li>• Therapeutic interventions</li><li>• Monitoring</li><li>• Health technology assessment</li><li>• Clinical studies/ surveillance</li><li>• Drug discovery/ development/ delivery</li></ul>	<ul style="list-style-type: none"><li>• Public Health</li><li>• Health care policy aspects</li><li>• Disease management</li><li>• Rehabilitation</li><li>• General health &amp; hospital care</li><li>• Gerontology</li></ul>

Initially, starting with the first ESFRI Roadmap, the focus of the BMS Group was on the medical sectors – the first generation of BMS RIs makes this focus obvious. The second generation already has some outstanding examples for biological resources. Future BMS RIs will hopefully contribute to the coverage of the whole range and fill some of the existing gaps in the BMS RI landscape.

During the update process, the BMS TWG was well aware, that its scope has various interfaces if not overlaps with those of other ESFRI Working Groups: ENE – Energy; ENV – Environmental Sciences; and SSH – Social Sciences and Humanities as well as the e-Infrastructure Reflection Group (e-IRG).

BMS TWG will continue to encourage further cooperation and networking between initiatives beyond those already established

and in some cases substantiated with agreements (see Figure 1 and Chapter 4 “Progress of BMS RIs”, Table 18 “Links between the Research Infrastructures”).



**Figure 1:** Overlaps/links between respective ESFRI Groups



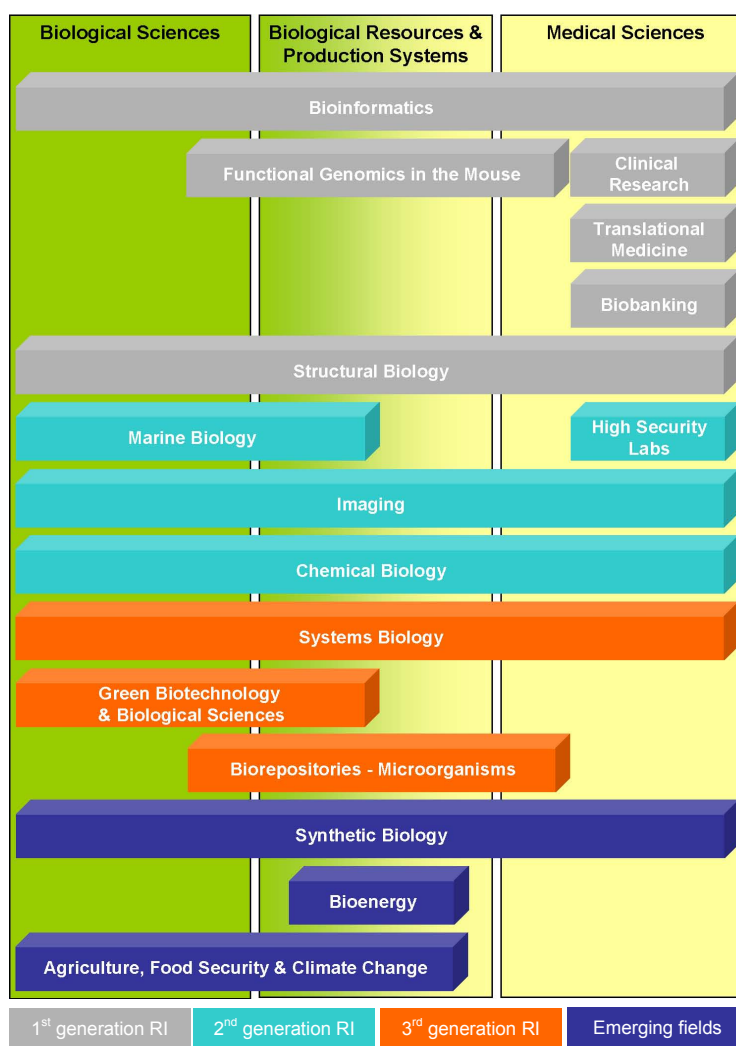
### 3 THE EUROPEAN RESEARCH INFRASTRUCTURE LANDSCAPE (ERIL) IN BMS

#### 3.1 ESFRI BMS Scientific Landscape

The ESFRI BMS Scientific Landscape is a detailed description of the various fields of research underpinned and supported by BMS RIs (see Figure 2). The rapidly changing and evolving BMS Scientific Landscape, a result of the increasing knowledge economy, means that those RIs put in place must now be adaptive to new scientific advances and flexible to these changes to ensure that they are embedded in their respective fields. In this capacity, BMS RIs will continue to function as the framework and support for the

European knowledge triangle – providing excellent scientific research, education, training, and open innovation, and for tackling global Grand Challenges.

It is in the context of the ESFRI BMS Scientific Landscape, the European knowledge economy and the global Grand Challenges, that the current portfolio of BMS RIs is discussed. This chapter also considers the demands that future RIs must meet and the gaps in the ESFRI BMS Scientific Landscape. Finally, future perspectives for BMS are introduced to highlight new and exciting developments in the Life Sciences community.



**Figure 2:** Scientific landscape of BMS RIs

### 3.1.1 Cross-Cutting RIs and Biological Sciences

The 10 BMS RIs on the Roadmap each encompass facilities, technologies and excellent scientific knowledge that are complementary with one another. The scientific areas that they cover are cross-cutting, a property intrinsic to all RIs. The harmonised BMS RI landscape creates a unique research environment, which will attract world-leading researchers and experts from outside Europe to perform cutting-edge research in an ERIL to reach the ERA. BMS RIs will overcome the fragmentation of the European Biological and Medical Sciences research landscape and provide researchers access to world-class research facilities. Each of the BMS RIs, separately or jointly, addresses the global Grand Challenges in several ways.

The BMS ERIL with its coordinated approach of the BMS RIs will deliver synergies and highly interoperable processes resulting in a value generating chain without gaps and rapidly translating findings from basic research to new medicines. These markedly reduced research and development timelines will result in faster publication, improved securing of intellectual property, and faster market entry of new products; thereby improving the health and wellbeing of European citizens and leveraging Europe's competitive edge in the global market.

Pharmaceutical as well as medical diagnostics research and development are facing substantial challenges that have prompted the industry to shift from the vigorous pursuit of intellectual property towards exploration of pre-competitive cross-industry collaborations and engagement with the public domain. High-quality, open and accessible resources, data and facilities are the foundation of pre-competitive research, and strong public-private partnerships have considerable potential to enhance R&D. The BMS RIs will provide the appropriate environment to establish public-private partnerships that will enable the construction of "expert centres". These will provide trans-national access to high quality resources, data and expertise for academia and industry, while retaining

the direct engagement of commercial interests in Europe.

Another key activity of BMS RIs will be the training and education of future professionals for R&D in close cooperation with other European and global training programmes. The effective operation of BMS RIs will rely on their ability to foster, build and maintain human capacity. BMS RIs will provide unique research environments that will equip individuals with the skills and access to information, knowledge and training, and will attract and retain researchers, engineers and technologists from different countries, regions and disciplines. The BMS RIs rich environment is based on the diversity of human resources available in the ERIL, and will strive to maintain such diversity and constitute a pole where training is centralised and multidisciplinary networks are built.

In the future ERA, the BMS RI landscape forming the ERIL will create a framework for efficient interaction of leading scientists and cutting edge technologies from various disciplines thereby facilitating the generation of ground-breaking innovation. The following cross-cutting areas are therefore described from the infrastructural point of view. They aim to provide a context in which BMS RIs are developing and to which BMS RIs will respond to enable the successful establishment of the ERIL.

#### Bioinformatics

Bioinformatics uses computer science, engineering, and mathematical methodologies to manage, visualise, and analyse biological data. Database development, data management, software development, modelling, and quantitative analysis are the main pillars of this science; the combination of which leads to new discoveries of biological patterns and the construction of hypotheses and models, which serve to advance biological research.

The two disciplines medical informatics and bioinformatics differ in their histories, scientific foundations, and methodological approaches; however for the purposes of this discussion they are not considered separately. Indeed, there is a high degree of complementarity and commonality between

these two disciplines, both around the tools they share and the complexity of the challenges they face. It is expected that, with time, medical informatics and bioinformatics will become more and more integrated, with infrastructures playing a key role in facilitating this process.

Bioinformatics serves to save, assemble, organise, integrate and disseminate information covering all biological, spatial and temporal scales. Data is, therefore, generated in a wide variety of formats and from diverse disciplines and the current demand is to respond effectively to new and rapidly evolving data and information needs. The generation of data from Life Sciences is increasing at unprecedented rates and represents a challenge to bioinformatics. It deciphers the genomic, transcriptomic, and proteomic data generated by high-throughput experimental technologies as well as data derived from the systems approach and organises information gathered from traditional biology and medicine. The size of biological datasets, and the knowledge generated by the data is now escalating to the point of becoming unmanageable and is demanding more and more the provision of large memory space and enormous computation capacity and time.

Researchers need data to be longer-lived and more valuable, and require data to validate methods and models and to answer new, complex questions that involve multiple factors. Data should therefore be accessible, accurate and integrated in order to increase understanding and to allow informed-decision making. Instruments and policies must continue to develop so that the mobilisation, sharing, and exchange of data and knowledge are enabled, supported, and facilitated to the maximum benefit of the scientific community. Information that is useful and truly accessible to all should also maximise full intellectual and commercial exploitation.

A limiting factor to progress towards data mobilisation and sharing is the lack of understanding between those who develop bioinformatic tools and those who use them. Bioinformatics is conducted by a specialised group of individuals, such as database curators, database and software engineers,

and computational biologists, while biologists often remain outside problem-solving issues. It is therefore highly desirable that biologists develop basic skills such as database development and management of large datasets, and quantitative and statistical analysis of data as part of their training. Coupled with this, there is a need for developers of bioinformatic systems to engage with biologists to better understand how biological data is generated and used. A culture shift of social integration will allow these communities to talk to each other and work together.

Considerable efforts are required to provide the necessary high-performance computing, sophisticated algorithms, advanced data management capabilities and training so that the automatic operation of data integration and knowledge extraction from data becomes a reality. Such advances would increase data usability and analysis at industrial scales. A concerted approach to bioinformatics would minimise overlapping and therefore wasted resources where computational tools and solutions are reinvented by different users, and would prioritise support for the curation of worthwhile datasets and the sustainability of worthwhile software.

Turning these advances into innovation in and for the ERA requires an integrated and inclusive approach that maximises national investments and scientific efforts, and the appropriate infrastructure that enables integration and interoperability of highly diverse datasets being generated in the ERA. The European Life Sciences Infrastructure for Biological Information – ELIXIR – seeks to address the challenge to cope with the volume of data generated by the high-throughput revolution and with the high demand for rapid access to public biological databases, and to obtain the full value from these advances through collecting, integrating, storing, curating and disseminating data for their maximum use and exploitation in the ERA.

### **Bioimaging**

Cutting-edge bioimaging technology is a rapidly advancing field in the life and medical sciences and holds great promise for improving patient care. Together with the

“-omics” technologies, databases, and biobanks, the innovative imaging techniques are key tools for scientists studying living systems at the molecular, the cellular and the organismal level. They provide essential information on how life is organised from single cells through tissues and model organisms to humans. Bioimaging therefore services all scientific fields from basic cell and developmental biology to biotechnology and medicine. The challenge facing biomedical imaging is twofold: to translate the tremendous achievements of molecular biology into early diagnosis, efficient follow-up of therapeutic treatments and prediction of therapeutic response; and to develop novel imaging-guided drug delivery and minimally invasive treatments.

The development of advanced light microscopy methods and biomedical imaging with the use of digital imaging technologies has rapidly advanced over the last decade. Laser-assisted fluorescence microscopy provided the researchers with the tools for precise 3D visualisation of the biological samples with an unprecedented resolution. Abbe's law for diffraction limited resolution in light microscopes (~0.5 micron), which was regarded for a long time as insurmountable, has been overcome by the advanced laser imaging techniques. Stimulated emission depletion (STED) microscopy can now facilitate imaging of objects of several tens of nanometers. This means that optical imaging is moving into domains once solely reserved for the electron microscopy. Light microscopy is no longer simply the technique for static imaging of biological objects. Various methodologies, such as fluorescence correlation spectroscopy in combination with confocal techniques allow the researcher to visualise and monitor the complex dynamics of many processes inside living cells. Development of highly sensitive photon detectors opened up new avenues for investigation of biologically relevant events at a single-molecule level. In addition, the use of optical tweezers in combination with high-resolution optical imaging provides researchers with exceptional technological capabilities of manipulation of the biological samples at the sub-cellular level. Novel non-fluorescence based approaches and detection systems, such as Coherent Anti-strokes Raman Spectroscopy (CARS) and

Surface Enhanced Raman Spectroscopy (SERS) microscopy methodologies are becoming increasingly relevant for biomedical imaging. Despite significant advances in light microscopy there remains an unmet need for non-invasive high resolution imaging techniques without the high-energy radiation burden, which can help to accurately predict, diagnose and monitor therapeutics and treatment procedures in patients at the tissue, cellular and subcellular levels. Until now light microscopy, with few exceptions, has been restricted to the examination of the tissues and organs in *ex vivo* or post mortem conditions. Although fluorescence microscopy has proven to be one of the most powerful tools in biology, its application to the intact animal has been limited to imaging several hundred micrometers below the surface. Recent developments in non-linear spectroscopy imaging techniques in parallel to the discovery of quantum dot fluorescent probes including near-infrared fluorescent agents demonstrate possibilities of tracking cells and visualising tissue structures deep inside living organisms.

The advancement of the high energy irradiation methodologies generated a whole spectrum of versatile and extremely sensitive clinical anatomical imaging techniques such as computed tomography (CT), positron emission tomography (PET) and single photon computed tomography (SPCT). PET allows the *in vivo* visualisation of pathophysiological processes by specific molecular probes down to the cellular level: this allows the researcher to monitor specific actions of new therapeutic agents in fields of oncologic, cardiovascular and neurodegenerative diseases. The invention of magnetic resonance imaging (MRI) revolutionised how complex internal structures and functions of the body are visualised and provided minimally invasive means to detect and monitor pathology induced tissue and organ transformations. MRI, which many clinicians are familiar with, has become the most generally used imaging modality for medical diagnosis. Conventional MRI is only the first of an array of methods that will eventually comprise the nuclear magnetic resonance (NMR) diagnostic armamentarium. The development of high field MRI that simultaneously allows fast morphological

analysis, diffusion and perfusion imaging, functional imaging, magnetisation transfer imaging and biochemical analysis (NMR spectrometry) has contributed to clinical research in all fields of medical sciences. Emerging techniques such as ultra high field MRI as well as phase-contrast CT methods will further improve tissue contrast and will non-invasively resolve *in vivo* structures down to the microscopic level. In addition, more specific contrast media will also enhance insights into the pathophysiology of disease.

Such sophisticated instruments are, however, costly. Initial purchase outlay costs are high with most instruments requiring consistent maintenance and eventual upgrade, in addition to the specialised infrastructure required for operation and support.

The funding and human expertise required to establish and run the infrastructure considerably exceeds the financial and the scientific capacities of an individual laboratory or a single institution, and most individual national research funding bodies. These factors mean that individual scientists in individual countries across Europe may not be able to access and utilise the full power to these technology developments. Implementation of a concerted European effort in biomedical imaging facilitated through a strong cooperation between the Member States, coupled with a simultaneous drive to coordinate building technological capacity for bioimaging, will provide access to the latest technology and expertise for scientists across Europe.

The RI Initiative Euro-BioImaging for imaging technologies in biological and biomedical sciences will bring together key research areas in imaging technologies ranging from basic biological imaging with advanced light microscopy, *in vivo* molecular imaging of single cells to animal models up to the clinical and epidemiological level of medical imaging of humans and populations.

### Structural Biology

The atomic level structures and interactions of proteins and macromolecular assemblies dictate their function. The field of structural biology provides detailed insights into the

interplay of structure and mechanism of action. Thus, structural analyses build conceptual frameworks which support a wide-range of functional studies and provide very specific information enabling a rational approach to the manipulation of protein function and interactions. This field therefore interfaces with many aspects of biological and clinical research and illuminates in molecular detail the function of cells.

Structural biology is undergoing a number of most interesting developments. The maturity of the classical tools, such as X-ray diffraction (XR) and NMR has enabled widespread use to most department or institutions. This general incorporation has been followed by the broadening of new possibilities derived from the use of improved equipments and experimental methods (smaller diffraction focus, robotized sample loading and automatic analyses implemented at the synchrotrons, more powerful magnets and improved pulse operations, etc). Furthermore, the incorporation of several other key actors to the scene has positively modified the scenario: electron microscopy (EM), mass spectrometry and biocomputation have evolved in recent times to interface XR and NMR in such a way that it is likely that the most exciting developments will be derived in the near future from the integrative use of several of these methods to solve the structure, interactions and functions of complex cellular components.

EM, for example, lies at the interface between structural biology and bioimaging. Within structural biology the development of techniques such as cryo electron microscopy and tomography are used to link with molecular structure, thus complementing XR and NMR to tackle the study of large complexes. The incorporation of XR data from structural components into large EM volume reconstructions is presently a main workhorse in the analysis of the cellular interactome. Quasi-atomic maps obtained through this approach can be complemented with small angle X-ray scattering (SAXS), nanospray mass spectrometry, and others, such as surface plasmon resonance which, together with computational docking and modelling, are expected to yield unprecedented insights into the structure, dynamics and functional

aspects of important biomedical macromolecular complexes. The correlation of structural analyses with single molecule manipulation methods (atomic force microscopy, magnetic and optical tweezers) is also an interesting aspect to be considered in future developments for integrative infrastructures.

Some of these new correlative approaches will be integrated into structural genomics initiatives. Although not all offer suitability for large throughput scaling, there are great possibilities for the incorporation of extended analysis of minute amounts of samples based on the progressive incorporation of automation and robotisation, as well as on the extension of nanotechnology to provide nanoreactors based on microfluids and synthetic tools.

Moving towards the molecular and atomic domain is not the only present trend in structural biology: Structural cell biology is the new frontier where the advancement of new and powerful equipment related to light microscopy is rapidly interfacing to electron and X-ray tomographic microscopies. Improved optical super-resolution and energy transfer based methods are paving the road to correlative microscopy, whereby a cell can be studied under physiological conditions, then, followed by localisation of specific structural components, with interactions detected up to the single molecule level. Determination of the topological relationships with other cell components and resolving structures down to the molecular level will complete the structural and functional atlas of each cell type, and facilitate assessment of cellular modifications under specific biomedical conditions. To achieve these goals efforts must be supported to develop integrative infrastructures capable of interfacing these novel correlations.

Last, but not least, it is becoming evident that integrative structural biology is a big data science: handling the quantity of data being produced is a main biocomputational task. The analysis, correlation and exploitation of all these correlated data under conditions which facilitate their universal access are clear objectives of several ongoing projects, not only in Europe, but in USA and Asia. The incorporation of integrative structural biology to structural

genomics and system biology will demand an increased computational development specific for these purposes.

The European BMS RI INSTRUCT is a distributed centre for integrated structural biology that is expected to consist of seven core centres, each with a broad complement of core technologies and also specific expertise. INSTRUCT will facilitate a pan-European network of centres that will integrate to obtain multi-scale structural data and translate these data into functional knowledge.

### Chemical Biology

Chemical Biology is an emerging scientific field covering the interface of chemistry and biology that involves the application of chemical techniques and tools, often compounds produced through synthetic chemistry, to the study of biological systems. The use of chemical tools to explore biology provides unique means to unravel complex biological processes by directly probing living systems at the chemical level. As a major goal, chemical biology aims to identify small-molecule modulators for individual functions of proteins; this will enable a deeper exploitation of the wealth of genomic information. Chemical biology brings together molecular biologists, chemists, engineers, and bioinformaticians and creates numerous opportunities for basic science, translational research and clinical medicine. Chemical biology focuses on understanding biological systems at the molecular level and using these mechanistic insights to expand chemistry and biology in new directions. Using diverse experimental and theoretical techniques, chemical biologists have tackled challenging problems in biology, ranging from cellular signalling to drug development and neurobiology. Testing small molecule libraries for biological interactions with disease-related protein segments could speed up drug discovery.

With the completion of the human genome sequencing, advances in biological research have grown exponentially. The use of genetic knockouts, RNA interference and site-directed mutagenesis to understand the roles of genes and proteins has contributed significantly to our basic understanding of

biological functions. With the use of chemical genetics, biologically active compounds are now being used as another means to address difficult biological questions. Small molecules offer a significant number of advantages over classical biological approaches to knock out or inhibit the action of specific proteins at any desired time. In this approach small molecules act as conditioned alleles to answer biological questions that are difficult to study with standard genetic methods. In contrast to research using biochemistry, genetics, or molecular biology, where mutagenesis can provide a new version of the organism or cell of interest, chemical biology studies probe systems *in vitro* and *in vivo* with small molecules that have been designed for a specific purpose or identified on the basis of biochemical or cell-based screening. Despite the expansive research interests of chemical biologists, the overall goal is to understand and manipulate living systems at the molecular level with increasing precision. This is a subtle difference from biochemistry, which is classically defined as the study of the chemistry of biomolecules. Exploration in the field of chemical biology has benefited modern drug discovery. One domain of chemical biology, rational and structure-based drug design, is a powerful approach to the discovery of new drug targets. Advances in modern technology have made crystallising a protein and elucidating its 3D structure more straightforward. This has allowed the structure of proteins to be studied at the molecular level by chemists, a development that has resulted in this innovative topical research area.

The efficiency and the impact of the approach depend largely on the availability of a diverse and well designed chemical compound collection, the most advanced screening technologies, chemistry resources, special cell line collections, bio- and cheminformatics capacities, and a comprehensive database. To build upon this excellent foundation, the current scientific leaders of chemical biology need to step forward to coordinate broader initiatives to advance the community in the coming decade. Thus, in contrast to what is common in many biomedical scientific disciplines, researchers working with small molecules often use tools normally

associated with industrial drug discovery. Synthesis of a large number of compounds is done with efficient large-scale technologies while bioassay testing of the molecules is done with high-throughput screening.

A European central chemical biology facility will make available a large collection of diverse compounds representing the chemical knowledge of Europe. The ESFRI EU-OPENSREEN chemical biology initiative will allow researchers in academia and small and medium-sized enterprises (SMEs) to access resources for the development of bioactive small molecules. It will be an association of high throughput screening centres. Such facilities are expected to accelerate generation of knowledge in the fields of translational and clinical medicine together with our general understanding of basic knowledge of biological functions. EU-OPENSREEN aims to satisfy the needs for new bioactive compounds in many fields of the Life Sciences; for example human and veterinary medicine, systems biology, biotechnology, agriculture and nutrition.

### Systems Biology

Systems Biology is the emerging major scientific concept that will greatly facilitate the exploration of the organised complexity of life. Most biological processes involve network interactions between multiple genes, proteins and environmental variables. Understanding how biological function and diversity emerges from interacting biological components is the major challenge for modern biology and lies at the core of developing systems approaches. The complexity of these interactions in time and space is enormous, creating highly individual and variable responses necessitating the integration of experimental quantitative data on a systems-wide level to obtain information about the state, dynamics and variability of living cells, organs, organisms and populations. The goal is to standardise these approaches and integrate them into predictive models. This phenomenon pertains to the understanding and promotion of health and the retardation of ageing, as well as to diagnosis, e.g. through novel biomarker strategies, and therapies, e.g. using new network targeting drugs, of

disease. Attempting to unravel and understand the dynamics of these processes requires the collection and integration of experimentally-derived quantitative systems-wide data on the state, dynamics and variability of living cells, organs, organisms and populations. Handling and interpreting these diverse datasets demands the use of a variety of computational, mathematical and statistical modelling techniques and can only be achieved with a critical mass in both the experimental and quantitative sciences.

At this rapidly increasing pace, advances in modern molecular biology, biotechnology and medicine are driven by interdisciplinary research which integrates experimental molecular biology, clinical research, bioinformatics, computational biology, mathematics, computer science, physics, chemistry and biological engineering in an approach termed systems biology. Systems biology is the new way of doing science, demanding new intellectual and organisational structures to deliver its full potential. This integration can only be achieved through a certain critical mass of experimentation, such as in genomics, proteomics, metabolomics, RNA-omics, lipidomics, interactomics, etc. With the help of mathematical analyses, modelling, informatics and statistics they will generate predictive models of complex biological processes.

Biological networks, both intracellular and in-and-between whole cells, tissues and organisms, connect thousands of molecular and higher-order functions, such that functioning of any part of the network depends on different, remote parts. Most interactions are “nonlinear” such that the function they generate depends on the precise strengths of the interactions and on the state of the system. Systems biology can be applied to elucidate complex networks ultimately as large as entire expressed genomes, or to more precise functions, to experimentally determine interactive properties of molecular constituents, which is novel for the engineering and physical sciences. Systems biology can then be applied to connect the molecule to application, within clinical and biotechnological settings. The task of systems biology is to transform data into

predictive models of life in health and disease through the integration of experimental, computational and theoretical approaches.

European science has the inherent ability to achieve these objectives in principle, but there is no infrastructure in place to integrate the existing fragmented efforts. A key objective will be to bring focus to these disparate efforts by supporting large-scale research projects on major areas of urgent need in medicine, the biosciences and the economy - for example, human physiology and ageing, complex diseases, bioenergy and biomanufacturing. However, these activities require specialised infrastructures dedicated to systems biology. The use of computer models and systems analysis will transform our current basic, fragmented knowledge of complex molecular systems into an integrated dynamic approach that can be applied across a variety of biological and biotechnological fields. These are as diverse as the evolving area of predictive, preventive and personalised medicine, biofuels and ecology.

The ability to have a significant impact in these areas is currently beyond the capability of any single European Institution. Coordination of effort through a European systems biology infrastructure will address this and will also provide support to individual laboratories and smaller and medium size consortia that have succeeded in national or European grant applications. Coordination will also facilitate efficient interaction between the substantial investments in systems biology already made by national programmes, e.g. Biotechnology and Biological Sciences Research Council (BBSRC), Bundesministerium für Bildung und Forschung (BMBF), EU, European Research Council (ERC), the Netherlands Organisation for Scientific Research (NWO), and the Swiss Initiative in Systems Biology (SystemsX.ch). This infrastructure will be of particular benefit to less well-funded groups in the emerging economies of some Member States. Each individual laboratory will benefit from the step-change in the quality of science achievable through provision of an integrated infrastructure and the organisation and management which will ensure the continued development and



sustainability of this infrastructure. This will be particularly true in relation to Member States in Eastern Europe. A robust, open, transparent and competitive process will be put in place to define the management and organisational structure and its membership. Finally, such a focused European infrastructure will offer a single point of contact for access to a network of best practice in systems biology, unique in the world, stimulating contacts with non-EU consortia from academia, industry and regulatory agencies across the globe, as well as other related infrastructures and programmes within the EU (for example the Innovative Medicines Initiative (IMI), Integrated BioBank of Luxembourg (IBBL), BBMRI, EATRIS, ECRIN, ELIXIR, Euro-Biolmaging, INFRAFRONTIER).

### Synthetic Biology

Synthetic biology is an innovative and growing field which, by applying the principles of engineering to the biosciences, seeks to design and construct new biological parts and systems, and to redesign existing biological systems to deliver novel functions that do not exist in nature.

Synthetic biology is highly interdisciplinary, bringing together biologists of many expertises, engineers, chemists, physicists, computer scientists and many others to achieve an unprecedented insight into how biological systems function and how this can be improved to optimise certain biological activities. Building on the powerful research originating from recombinant DNA technology, genome sequencing and proteomics analysis, it aims to significantly deepen our understanding of the origin and function of living systems and to rebuild them to work better in the context of a wide range of biomedical, agricultural and food science, and environmental applications.

The hierarchy of synthetic biology components, where interventions can be made, includes the set of basic units, i.e. amino acids, nucleic acids, sugars and lipids; programmed molecular components and nanoscale building blocks; self-assembled units; peptides and proteins; functional proteins and DNA tertiary and quaternary structures; interacting networks of functional assemblies, i.e. systems; and

encapsulated complex systems, i.e. cells. This vast range of components is used in many approaches, which can be broadly grouped as: genome engineering, e.g. the construction of synthetic chromosomes for whole or minimal organisms; biomolecular engineering, e.g. biobricks or toolkits of functional units; biomolecular-design, i.e. *de novo* design and combination of biomolecular components; and protocell-design, i.e. self-replicating, encapsulated systems made from entirely synthetic components.

Unique to synthetic biology are its engineering principles, which provide the foundation to support reliable building, testing and programming of biological function. The high degree of standardisation of biological parts, devices and systems suggests that biological systems have the potential to be designed and constructed at a pace that is similar to that of other technology sectors. The Registry of Standard Biological Parts, founded in 2003 at the Massachusetts Institute of Technology in the US, is a collection of genetic parts that can be mixed and matched to build synthetic biology devices and systems. The Registry provides a resource of available genetic parts to international Genetically Engineered Machine competition (iGEM), iGEM teams and academic laboratories. At present, there is not an equivalent repository in Europe; however, there is scope for BBMRI or emerging infrastructures to consider hosting a registry with complementary components.

Potential applications of the field are diverse and promise to offer societal, environmental and medical benefits: vaccines and pharmaceutical drugs; biosensors; bioremediation; cell factories; biomaterials; gene therapy; biofuels; food ingredients. There is a great potential for the creation of technology platforms on which researchers develop tools, provide training, and create new products in collaboration with industry.

As the development of tools and technologies for engineering biology progresses, appropriate strategies and measures are being established to assess the impact that such technologies will have on the creation of biological risk, and to ensure that tools and technologies are built

alongside specific approaches to risk management.

Intrinsic to synthetic biology is the aim to increase our understanding of the origin and function of biological systems. Both the scientific community and funding organisations agree that these applications can only be developed successfully and to their full potential if the Ethical, Legal and Societal Issues (ELSI) associated to them are considered in parallel and are resolved at an early stage. ELSI considerations have been embedded in several national policy development activities for many years, for example in the UK, Austria and the Netherlands, and are being used to inform future policy and funding decisions and to raise public awareness and stimulate constructive public debate. ELSI have also been part of a number of European activities and policies, e.g. BBMRI, Towards a European Strategy for Synthetic Biology (TESSY), Safety and Ethical Aspects of Synthetic Biology (SYNBIOSAFE), Coordination puts synthetic biology on firm footing (EMERGENCE), and European Group on Ethics (EGE).

### 3.1.2 Biological Resources and Production Systems

Two main scientific areas provide the springboard for a huge leap forward in our ability to understand and to work with biological systems.

The first area concerns the remarkable advancement in our substantial understanding of the molecular, cellular, genetic and developmental basis of life, largely derived from the reductionist approaches over the last century or more and greatly accelerated by access to understanding of the genomes of human and model organisms.

The second area is that of high-throughput post-genomic technologies and e-science, which has enabled large-scale integrated approaches to apply the outputs of reductionist bioscience to the understanding of complex biological systems in “target” organisms – humans, animals, plants and microbes that sustain and enrich the quality of our existence. These areas, coupled with a vast range of biological materials and resources of the planet have been

assembled in Europe over the last 400 years, provide the platform for future bioscience research and challenges: this scientific opportunity arrives at a time when major challenges facing mankind require bio-based solutions (see below).

Biological resources that have been created so far became the basis of further research development in all main fields of BMS; in addition, new cross-interacting resources are appearing from disciplines that influence human and animal environment. These cross-interacting systems have to be understood since they provide the basis for the progression of biotechnology and human health as well as the improvement of biological production systems.

### Biological Resources – genetic and biological resources

Genetic and biological resources such as gene libraries, gene clone and cell-type collections, recombinant proteins, antibodies and affinity binders, and model organisms are key resources and fundamental tools for various fields in biological and medical research. These resources are often established within publicly-funded national or European research programmes. However, storage, use and access to these resources is not always adequate or straightforward. Major investments that have been made into these resources are often ineffectively used or lost because of lack of sustained funding for long-term maintenance. Furthermore, access is typically provided for project partners but not for the European scientific community or industry, in general. This situation should be markedly improved since genetic and biological resources are central pillars of most of the BMS RIs.

Human biological materials and resources that are required for the investigation of human diseases are the major focus of BBMRI, EATRIS, and ECRIN. Therefore these initiatives will become the key infrastructures for biomarker discovery and development thereby essentially contributing to the advancement of personalised medicine and to improve the efficacy in drug development. These biomedical infrastructures could build on knowledge sequent upon INFRAFRONTIER that focus its activity on the attribution of the function of

all individual genes in their complex networks.

INFRAFRONTIER aims to gather valuable knowledge on basic human gene function using the mouse as a model organism. The mouse is genetically very close to humans and therefore an ideal model for physiological functions and disease processes in humans, and to test new drugs and treatment strategies.

The number of mouse models of disease is increasing year on year and will continue to increase as our knowledge of genetics, genomics and pharmacogenomics grows. All of these models require systematic characterisation at the functional and molecular levels and should be made available to the entire European research community. These increasing demands for characterised mouse models are surpassing the capabilities of individual or indeed national research facilities, where economic and capacity restrictions apply. INFRAFRONTIER will bridge this gap, providing a distributed pan-European infrastructure that will facilitate standardised, high-throughput phenotyping and archiving of mouse models and efficiently distribute the mouse models to the scientific community. Implementation of INFRAFRONTIER will ensure Europe keeps pace with world-wide progress on the attribution of gene function.

The endeavour of INFRAFRONTIER to build one of the most comprehensive genetic resources of mammalian gene mutants that as mouse models or embryonic stem cells raises a number of opportunities and challenges for the biomedical sciences community. Systematic and comprehensive phenotyping of the mouse mutant resource will generate a rich dataset that will enormously enhance understanding of human disease processes, and provide the resources to elucidate complex gene networks that control developmental and physiological functions. However, this goal is not without many formidable obstacles that will require innovative and cost-effective solutions in phenotyping development, standardisation of protocols and informatics. To strengthen its effort INFRAFRONTIER became a part of with the newly established International Mouse Phenotyping

Consortium (IMPC) that strives to unify the efforts on building the largest mouse genetic resource. The global effort of IMPC will build an open-access to databases of genes and plans to knock out or deactivate individual genes of the 20,000 found in the mouse genome and perform basic phenotyping of all gene mutants within a decade.

Whereas the mouse model is central to INFRAFRONTIER other ESFRI initiatives also assign biological functions to the identified genes in humans (BBMRI, EATRIS), animals (INFRAFRONTIER), microorganisms and plants (MIRRI, EMBRC, ERINHA). This functional annotation of genes impacts development of all scientific biomedical fields, from genetics to application research in human health, food or bioenergy production. There is a big application potential in marine organisms that collect genetic resources addressed by the RI for microorganisms.

All these biological resources have several features in common that make proper coordination across Research Infrastructures obvious. For instance, the proposed ERINHA RI in cooperation with BBMRI and other RIs will provide a unique framework to investigate pathogen-host interactions and will help Europe to efficiently respond to emerging pandemics and bioterrorism.

The Scientific Collections International (SciColl) initiative, proposed under an activity of the Global Science Forum of OECD, is directed at large-scale facilities that are critical for the conduct of research on global issues, such as food security, public health, and the conservation of biodiversity and ecosystems. The Global Science Forum aims at coordination of scientific collection-based institutions as part of a global RI. The scientific collections under the SciColl initiative relate to different materials including animals, plants, fossils, sediments and ice cores that have been collected in different contexts and time-frames to the biological resources of the BMS RIs. Nevertheless, important synergies and complementarities with respect to preservation technologies, access and their use in research projects exist that are relevant to all RIs. The integration of different types of collections and biological

resources will enable research on highly complex topics such as long-term effects of environmental changes on living organisms and human health.

### **Animals – production, health, welfare, and livestock management**

One of the key challenges in biomedical research in the post-genomic era is to attribute biological functions to the identified genes in humans, animals, microorganisms, and plants and utilise this knowledge to secure growing needs for food production, maintaining the biodiversity as well as adequate response to the climatic change. In addition to INFRAFRONTIER that creates mouse models and aims in functional attribution of all individual genes as a base for human studies, new emerging infrastructures are also aware of use the genetic information to solve conceptual aspects of biology to improve and optimise animal production in agriculture. The latter effort plans to gather information on animal nutrition, physiological background for digestion, and also basic knowledge of animal immunology with the aim of improving disease resistance and health.

No coordinated animal biobanks, large-scale facilities or national and international networks are currently available in Europe. Small and specific collections are generally located at distinct institutions and each one is managed by researchers and local staff. Currently, the biological resources are provided to academia, industry, some public and private laboratories and represent a support to the chain from basic translational comparative research to development and application of new diagnostic technologies and of emerging pathogens of interest for industry. The development of innovative antiviral vaccines, serological tests, cytotoxicity assays using continuous and primary cell lines, and the consolidation of expertise in the advanced diagnostic molecular fields are prominent examples.

Food, agriculture and biotechnology, and related areas should develop an effort to build up a European knowledge-based bioeconomy in view of the increasing demand for high quality food, which takes into account animal health and welfare. Especially, the needs being addressed by this endeavour are growing demands for

safer, healthier, higher quality food as well as sustainability and security of production (i.e. agriculture, aquaculture and fisheries). Also the increasing risk of epizootic and zoonotic diseases and of food related disorders is of great concern as outbreaks of major animal diseases can have a devastating impact on animal and human health, food safety, the wider economy, rural communities and the environment. Effective tools for controlling animal diseases are vital not only for Europe but also for the rest of the world. The above need calls for constructing new European infrastructure that will builds on existing infrastructures, resources and technologies (see chapter 3.2 “Identified needs for a new generation of Life Sciences RIs”).

### **Marine Biology**

Scientific progress in Biological and Medical Sciences relies on model organisms and discoveries of processes and components of biodiversity (from the level of ecosystems and species to metabolic functions and genes). Marine biological systems harbour the biodiversity components that are most unknown to science, and are therefore a resource in waiting to be mined. Some of the most striking recent discoveries of novel biodiversity resources are microorganisms associated to marine invertebrates, such as sponges, and those associated to extreme marine environments with unique conditions that are atypical for life on Earth such as deep sea vents, deep hypersaline anoxic basins or Polar Regions. Marine organisms also harbour the largest diversity of ancient evolutionary lineages on Earth, thereby having great potential for discoveries of unique evolutionary and metabolic processes, and associated genes.

The extraordinary progress in “-omics” research has started a new era of discoveries of marine biodiversity resources, their functional properties and potential utilisation to benefit humankind, as described in the “Marine Board Position Paper 15 on Marine Biotechnology”<sup>5</sup>. Such benefits include biological products for industrial biotechnology, biomaterials, drugs, applications in synthetic biology, for the food industry, and for the ecosystem services,

---

<sup>5</sup> [www.esf.org/marineboard/publications/](http://www.esf.org/marineboard/publications/)

some with key roles in regulating the Earth's climate systems.

A major challenge in the study of marine biological resources is access to “-omics” platforms, marine stations, research vessels and observatory sites that can provide the samples and experimental facilities for research on marine organisms from a wide range of marine evolutionary lineages and types of marine environments. The much needed marine biology infrastructure to address these needs must provide access to both cultivable model marine organisms and experimental facilities to manipulate them, and it must provide access to sampling of non-model taxa from a wide range of marine environments, particularly bioprospecting for industrial, environmental and medical applications. This aim can be achieved through an interaction between the established network of marine genomics-related research stations and marine sampling platforms of oceanic research fleets and other European stations in extreme environments (e.g. polar). Such an infrastructure must also include biological resource centres to archive collections of marine organisms and their associated biological elements (mobilome), genomics and transcriptomics resources, and associated information databases and computing power. This infrastructure must interact with database infrastructures in storing and providing access to the information that it will create.

An emerging field in the use of marine resources for food production through aquaculture requires infrastructural support to the application of genomics through marker assisted selection to selective breeding programmes, involving quantitative trait locus analyses and development of banks of gametes and embryos.

#### **Microbiological resources and production**

Microbial resources, when effectively used, are able to provide high quality resources that will enable Europe to make better use of its microbial diversity and contribute globally to answering the big questions of climate change, healthcare, food production and food security, and poverty alleviation.

A pan-European Research Infrastructure will provide resources and information to help resolve problems, improve production and provide protective measures. Countries of extremely rich diversity outside Europe and the envisioned globalisation of the network will provide to Europe facilitated access to the huge, mainly undiscovered resources. This initiative aims to provide improved services to identify and characterise newly discovered strains that will help drive biotechnological research and place Europe at the head of microbial based innovation and bioeconomy development. Its efforts will be strongly linked to initiatives being undertaken currently in Brazil, China, Japan, Kenya and Russia. The already established microbial resources need further enhancement to provide adequate support for research, innovation and discovery. Agriculture and food security are facing the important challenges of globalisation, consumer demands and environmental concerns.

Another concern is appearing in European microbial resource collections as the number of experts, mainly taxonomists is diminishing and most currently practising ones are approaching retirement age. Training new specialists and planning for the future will ensure continued access to this expertise needed to support new species discovery. Current databases of molecular data are incomplete and have erroneous data; co-ordinated action across the ERA using authenticated strains will ensure our future ability to identify and utilise new species. Such services are essential, as, for example biosafety, biosecurity and quarantine control is based upon knowing the name of the microorganism so that it can be compared to the controlled organism or pathogen lists. A Research Infrastructure dealing with microorganisms will strive to coordinate the output of such initiatives to protect investments by enhancing the capacity to store, add value to and deliver essential services.

#### **Plants – genetic and biological resources**

It is estimated that approximately 2 million samples (called “accessions”) of Plant Genetic Resources for Food and Agriculture (PGRFA) are conserved in gene-banks and germplasm collections in European countries. These collections represent about

one third of the global resources of plants conserved *ex situ*. In addition to these PGRFA collections representing the natural and cultivated variability, specific plant genetic material (recombinant inbred lines, mutants, populations, etc.) has been created in different laboratories across Europe to address scientific questions. Europe has a major responsibility in maintaining these resources in a sustainable way. They form the basis for crop research and breeding and are therefore essential to secure future needs for food and nutrition, and to address the emerging threat of climate change to our food production.

A number of European countries have developed an outstanding experience and capacity in the field of PGRFA research, conservation and utilisation. The development of sequencing, genotyping and phenotyping methods will allow the in-depth characterisation of these resources. Databases gathering information on sequence polymorphism, genetic maps, expression data, phenotypic data, etc., will increase the efficiency of the use of these resources in breeding programmes, in particular via the emerging genomic selection methods.

With the development of genomics, numerous biological resources have been and are still generated on different plants species, in particular Bacterial Artificial Chromosome (BAC) and expressed sequence tag libraries. In order to ensure their efficient conservation, distribution and use, it is of utmost importance to support a European centre providing a quality controlled conservation capacity and services such as generation of libraries, BAC pools, and screening of libraries to the scientific community. Clustering of the main European genetic resource centres in an ESFRI initiative will ensure the effective conservation and utilisation of the genetic resources in research and breeding programmes. It will also allow to standardise the methods of conservation and characterisation of these genetic resources and to avoid the unnecessary duplication of material.

### **Analysis of ecosystems for agricultural research**

In an era of dramatic changes in climate, land use and other human activities, understanding the responses of the biosphere to human drivers of environmental change is both an intellectual grand challenge and a practical necessity. Humans depend on a diverse set of ecosystem services like biomass production, including food, fibre, and fuel, and also depend on the maintenance of air and water quality. These services are strongly affected by human drivers and pressures of change such as climate change, land management, loss of biodiversity, air pollution, and water management.

An infrastructure for analysis of ecosystems should aim at developing a coordinated set of experimental platforms to analyse and predict the responses of ecosystems to environmental changes and to engineer management techniques to deal with these changes. This will be achieved by setting-up a distributed and coordinated network of well equipped state of the art *in situ* and *in vitro* experimental platforms associated with analytical and modelling platforms and linked to networks of instrumented observation sites. *In situ* Long-term Experimental Platforms should be distributed across the main types of climate and land use. Experimental approaches will assess effects of land management, climate and biodiversity. Long-term continuous measurements will be recorded for state variables of the system in conjunction with the biogeochemical cycles, fluxes to hydrosphere and atmosphere and the dynamics of biodiversity. A few Ecotrons, highly instrumented, will allow deepening our understanding of processes and testing specific combinations of forcing variables. The databases and model tools will also link this analysis of ecosystems to other European infrastructures and initiatives (EXPEER, LTER, and ANAEE), well beyond the BMS scope, to extrapolate the plot-level experimentation to larger scales.

The analysis of ecosystems could be driven by a newly emerging infrastructure that will provide services that are essential for excellent research on terrestrial ecosystems. A major need in agricultural research is to integrate experimentation with

large temporal and spatial scales relevant to the most pressing future drivers to achieve a better and more holistic understanding of the underlying processes. The availability of experimental facilities, very large data sets and the multi-functional measurements and observations of complementary platforms will allow a novel understanding of the dynamics of the state and fluxes within and between the most relevant compartments across a hierarchy of spatial and temporal scales. It will therefore contribute to the pan-European integration of excellent sciences and will bridge the existing research gap between monitoring and observational and functional experimental approaches, fully integrated towards modelling and prediction.

### **Impact of climate change on production systems**

The concept of climate change emphasises alterations in Earth's atmospheric conditions, particularly temperature, however also precipitation (rain, snow), cloud-cover in a time-frame of decades to centuries and beyond. The overwhelming evidence collected over many centuries demonstrate that human activity has greatly affected land use, and that industrialisation has resulted in substantial consumption of fossil fuels and rapid release and substantial accumulation of methane or carbon dioxide ( $\text{CH}_4$  and  $\text{CO}_2$ ) in the atmosphere. These changes in  $\text{CO}_2$  particularly are considered responsible for the observed increases in global temperatures. Climate modelling strongly suggests that increased temperatures will change precipitation patterns and amounts. Climate changes are the resultant of many processes, which may be considered as environmental change (i.e. not restricted to climate and atmospheric processes) affecting both the emissions of greenhouse gases (sources) and their consumption (sinks). All aspects of biosphere activity are involved, and ecosystems from the oceans to mountains, and from the soil with its micro- and macro-flora and fauna to the vegetation canopy. Human dominated (city/urban) ecosystems are not excluded.

Effects of environmental changes on biosphere productivity are multi-faceted and complex. There is two-way interaction between climate (weather in the short-term) and the biosphere. Environmental change at

the biosphere level affects weather and climate, which in turn exhibits a feedback, either negatively or positively, and also influences parts of the biosphere not responsible for the changes.

Climate change on the biosphere and biosphere's productivity are major objectives for predicting weather effect in long-term values. Accurate methods of forecasting would have considerable benefits in ecosystem management and human social and economic activities. For example, accurate fore-casts of the effects of temperature and rain-fall patterns on the distribution of plants and animals would help to evaluate the likelihood of ecosystem migration (e.g. movement of forests northward or to higher elevation with warming) or more specific effects on species (e.g. spread of plant and animals, pests, and human diseases and industrial activities). It is currently difficult to forecast the effects of the many inter-related weather and climate processes on the productivity of major parts of the biosphere because of the often limited, short-term and fragmented nature of the data and the inadequate nature of the tools for integration of information.

Addressing biosphere productivity will require attention to specific ecosystems, and to wider, major habitats, being the aquatic environment, predominantly marine but also fresh-water and the terrestrial natural, semi-natural and managed ecosystems, including forests, grasslands and pastures and arable agricultural systems.

Research Infrastructure in the agriculture domain should get more opportunities to address the challenges in the future. Agriculture sciences in Europe require technological development and integration, particularly in the environmental (soil, climate) interaction with crops. Understanding of the genetic, biochemical and physiological factors responsible for crop adaptation must advance to enable immediate applications of basic biochemical and physiological processes of significance in determining productivity.

Selection breeding of crop plants (with genetic inputs such as marker assisted methods) is an important route for adaptation of crop productivity to climate

change. There is substantial current effort in such topics by many national governments, with some investment by the private company sector. The feasibility of producing genetically-modified crops with specific beneficial traits is being explored. In light of the challenges humanity is facing to secure future food supplies, it is essential that all technologies are considered alongside any potential social, economic and policy issues they might raise. A major effort is required to re-focus scientific efforts on biosphere productivity, its determination by environmental and genetic factors, and how changing climate will affect it, plus what is required to optimise (or indeed maximise) crop productivity to ensure food security.

### Biological energy production

Bioenergy is a relatively new area of science. The term “bioenergy” encompasses the use of biological feedstocks as sources of energy. Europe needs to develop a variety of renewable energy technologies to meet its targets for reduction in greenhouse gas emission and bioenergy will be included in the future energy portfolio. The majority of renewable energy sources involve the production of heat and/or electricity; in contrast biofuels are currently the only source of liquid transport fuels, which can be derived from non-fossil sources. The advantage of using biofuels is that they can be used in existing vehicles using the existing fuel delivery infrastructure.

Europe has the potential for greater biofuel production but requires expanding research activities to achieve it. Current challenges in bioenergy include the development of new feedstock and/or the improvement of existing ones to enable growth of biomass crops on marginal land, with minimal water and fertiliser input, increased photosynthetic conversion, and better disease resistance. There is concern about the use of food crops as biofuel feedstock, which can push up food prices to unaffordable levels in developing countries. Current research focuses on non-food crops or agricultural waste, in order to reduce competition for land which might otherwise be used to grow food.

New methods are needed to convert the sugars in lignin and cellulose to free sugars which can then be fermented to produce

alcohols. This can include pre-treatment methods with low energy inputs and new enzymes for biological degradation of biomass. Biorefineries are also required to extract the maximum possible value from feedstock, which can yield high-value chemicals and materials as well as biofuels.

Developing networks of researchers who can share their results and resources will be important. Resources can include field sites, plant varieties, pilot plants for scale-up of fermentation and refineries.

As an example, the USA have developed large scale bioenergy centres such as the Energy Biosciences Institute and the Joint Bioenergy Institute, both of which bring together a large number of researchers from various disciplines. Europe has national bioenergy activities such as the UK's BBSRC Sustainable Bioenergy Centre but does not have any large-scale centres of excellence. It is worth considering whether such physical infrastructure is needed in Europe to enable the critical mass, human capacity, multidisciplinary research and innovation required to advance the field, or whether existing and emerging infrastructures have the capacity to host such activities.

The ability to locate and use such resources and facilities would be of benefit to researchers across Europe. There is also an opportunity to make use of existing facilities and resources which are currently used by existing researchers, e.g. plant and microbial cell lines, fermentation facilities. A European Bioenergy Network of Excellence exists, integrating the RD&D (research, development and demonstration) activities of eight leading bioenergy research centres, and there are many transnational collaborative bioenergy projects, but a better-coordinated strategy is required.

### Food and feed

In the year 2050 the global agrifood and biomass industry has to deliver double output with half the resources. This simple statement is the outcome of three challenges that implies a fundamental re-consideration of our current systems for production and consumption: (1) three planets are needed for food, materials and energy usage should the expected 9 billion



human beings follow a western consumption style; (2) obesity and related diseases are increasingly putting pressure on health care costs, especially in ageing societies; (3) shortage of clean water and oil threatens the full agri-food chain. Failure to overcome these challenges will result in further destruction of our ecosystem, a further bimodal distribution of hungry and obese people and collapsing health care systems.

These three societal challenges have been recognised by the European Commission and others, given the Joint Programming Initiatives on “Agriculture, Food Security and Climate Change” and on “Healthy diet for a healthy life” (see Chapter 2.1.4 “Increased relevance of RIs in the Life Sciences area”). However, taking up and dealing with these challenges is mainly done within isolation, in political terms, policy goals, business cases, up to R&D funding schemes, missing the fact that the three challenges are highly interrelated. Currently, first integrated visions and integrated R&D approaches are being developed. However, an integrated R&D infrastructure does not exist and is proposed by e.g. the working group on infrastructures of the Standing Committee on Agricultural Research.

The time has come to rethink and redesign the way food and biobased materials are traditionally produced. The first research and educational programmes are now being developed. The Collaborative Working Group under SCAR in the area of “shared infrastructures for European agri-food research” is proposing novel food facilities consisting of integrated R&D infrastructures, designed as a limited number of interlinked infrastructures with the state of the art equipment. These infrastructures should be composed of three inter-connected facilities: (1) “The Facility for Food and Health Research”, focused on combined real-life food body-uptake centre, online imaging techniques, and nutrigenomics tools (genome-wide transcriptomics and metabolomics-based phenotyping); (2) “The Facility for „Food Choice and Eating & Drinking Behaviour” that includes a brain-body (especially the mouth) centre for chewing and swallowing behaviour and for measuring facial expressions as criterion for product appreciation; and (3) “The Facility for the Production of Healthy Food and

Biobased products”, which represents the core of a cradle-to-cradle R&D facility for controlled resource input & product output experiments, i.e. input based on societal needs, business opportunities and nutritional.

### 3.1.3 Medical Sciences

Medical sciences cover all aspects of human health and disease. Within ESFRI the BMS TWG provides a platform for proper identification of the Research Infrastructures, which will secure development of health for European citizens through a combination of research and education at high international levels and to ensure the dissemination and exchange of research knowledge throughout the European healthcare field. The ageing population accompanied by decrease in the younger productive workforce and continuous increase in the cost of developing new medicines will markedly place pressure on the sustainability and viability of the EU’s healthcare and social systems. Furthermore, new threats to health have emerged such as pandemics and the risks of bioterrorism, which are globally recognised as important public-health issues. BMS RIs should form an integral part of the EU’s strategies to respond efficiently to these health-related challenges.

One of the major tasks in providing efficient health care to European citizens is therefore to improve current disease prevention opportunities and therapies. In particular, the right drugs have to be provided to the right patients at the right point in time. Furthermore, drug development has to become more efficient by avoiding the high attrition rate in the drug development process which directly translates into cost to be covered by the health care. As highlighted in the recent “Strategy Paper on the European Biological and Medical Sciences Research Infrastructures”<sup>6</sup> these goals can only be achieved by 1) better understanding of the molecular basis of diseases and how this relates to the genetic makeup of patients as well as its interaction with life-style and environmental factors, 2) improving diagnosis of diseases, 3)

<sup>6</sup> Meeting Europe’s Challenges: The Role and Importance of Biological and Medical Sciences Research Infrastructures, 2010

providing new drugs and medicines, and 4) improving the testing new drugs in patients for safety and efficacy. Moreover climate changes, increasing populations and increased mobility are major factors leading to the emerging of new pathogens with unknown risks for society and economy.

With the numerous recent breakthroughs in basic biomedical sciences, including human genomics, imaging, proteomics, structural and functional biology, stem cell biology, biomedical engineering, molecular biology, and immunology, among other disciplines they have provided an unprecedented supply of information for improving human health. This revolutionary progress in basic science would not have happened without the long-term investment in and steadfast commitment to basic biomedical research. Translating the information gained through these basic discoveries into knowledge that will affect clinical practice and, ultimately, human health requires a focused strategy within clinical research involving human subjects and human populations, as well as development of improved health services based on that research. This next scientific frontier including detailing the effects and consequences of interactions between environment (both chemical and mechanical) and genes in disease initiation and development deserves a corresponding investment and commitment. Without mechanisms and infrastructures to accomplish this translation in a systematic and coherent way, the sum of the data and information produced by the basic science enterprise will not result in tangible benefit for the European population.

### Biobanking

Biological resources – living organisms, cells, genes, and related information – are the essential raw material for the advancement of basic biological knowledge, biotechnology, human health, and research and development in Life Sciences (OECD 2001). Biobanks collect, store and provide access to these resources in a quality controlled and ethically and legally compliant manner. Human biological materials contain valuable information about genetic and non-genetic causes of diseases and on factors which influenced the disease outcome. Consequently, biobanks are required for improving disease prevention, diagnosis and treatment and are a

prerequisite for the development of new biomarkers indispensable for solving the attrition problem in the drug discovery and development processes. Biobanking is a specific strength of European research. However, Europe currently cannot exploit these potentials because of lack of interoperability of its biobanks that were mostly established in a non-coordinated manner at the Member State or local levels.

More than 250 biobanks of different formats localised in more than 20 countries throughout Europe can provide approximately 16 million samples to be used in basic research and drug development. Samples collected comprise mostly human tissues; DNA and plasma/serum, but newly established biobanks are focussing also on RNA, white blood cells, stem cells, urine etc. Several EU and worldwide projects (for overview on 25 EU-funded biobanking-related projects<sup>7</sup> were devoted between 2002-2010 towards harmonisation, quality management and cataloguing the existing biobanks and pertinent legislation. However, all the initiatives and major investments made into establishing biobanks suffer from the lack of sustainability and do not provide access on a European scale.

Currently, biobanks are falling into two main categories: a) population-based biobanks and b) disease-based biobanks, bringing together scientists of diverse fields, such as clinical medicine, human genetics, pathology, laboratory medicine, epidemiology, (bio)statistics, (bio)informatics, evolution, health economics, sequencing and genotyping technology, health economics, social sciences, etc.. Interdisciplinary and multi-national collaboration are the cornerstones of biobanking. No single biobank can provide the number of samples required for discovering the modest genetic effects that a single gene can provide on a complex trait or to support research on gene-environment interactions. However, apart from the high numbers of samples and data sets required, evidence-based standard procedures meeting the quality requirements of latest analytical technologies as well as internationally harmonised legal and ethical rules must be established. The current

<sup>7</sup> see [ftp://ftp.cordis.europa.eu/pub/fp7/docs/report-meeting-eu-funded-biobanks\\_en.pdf](ftp://ftp.cordis.europa.eu/pub/fp7/docs/report-meeting-eu-funded-biobanks_en.pdf)

heterogeneous landscape of biobanking-related legislation in European Member States is a major obstacle for Europe to increase its competitiveness in many fields of medical research.

The Biobanking and Biomolecular Resources Research Infrastructure (BBMRI) aims at building a coordinated, large scale European infrastructure of biomedically relevant, quality-assessed samples (with the possibility to link to related clinical and epidemiological information), to enhance therapy and prevention of common and rare diseases, including cancer. A specific challenge in this context is to build an interface between patients as well as populations of European countries and top-level biological and medical research. This can only be achieved in a highly distributed infrastructure with several operational sites in most if not all Member States. The construction of BBMRI not only requires innovative scientific and technical solutions for sample and data management but also has to place major emphasis on a broad spectrum of issues related to science and society.

### **Clinical Research**

Clinical research may be defined as a branch of medical sciences that through an overarching umbrella to dissect mechanisms in disease and their diagnosis, determines the safety and effectiveness of treatments, medications, interventions, and diagnostic procedures intended for human use. Information may be used to develop diagnosis, disease prevention and disease modifying treatment or for relieving symptoms of a disease. Moreover, clinical research refers to the entire biography of a drug from its inception in the lab to its introduction to the consumer market and follow up beyond. The promising candidate or molecule identified in the lab has to be subjected to pre-clinical studies including animal studies where different aspects of the drug, including its efficacy and toxicity, are studied.

The development of the European ECRIN-initiative is a European platform for the support of clinical research projects. It is based on the connection of national networks of clinical research centres and clinical trials units, and integrates national

clinical research facilities into a pan-European infrastructure, able to provide support to multinational clinical research in any medical field, and for any category of clinical research. ECRIN currently includes 12 networks in nine European countries representing a population of 350 million.

There is a need to freshen up the list of problems that should be addressed by the concerted activities of scientists, clinical representatives and patient groups/organisations such as participation in longitudinal studies. When fully established ECRIN will provide integrated “one-stop shop” services to investigators and sponsors in multinational studies, with the local contribution of staff embedded in each national coordination (patient recruitment and investigation, data management, GMP manufacturing of biotherapy products, quality assurance, monitoring, ethics, regulation and adverse event reporting). In addition, consulting will be provided to investigators and sponsors upstream to the study on issues such as regulation, ethics, centre selection, cost, funding, and insurance.

### **Translational Medicine/Research**

Translational research is a set of processes aiming to bridge the gap between laboratory discoveries and clinical medicine by harnessing and integrating advances in basic and medical sciences, and converting them into novel approaches for disease prevention, diagnosis and treatment, and also to provide feedback from clinical observations to experimental basic biology research.

Despite significant advances over the last decades in the understanding of fundamental aspects of human biology and the emergence of new powerful technologies, the transformation of this knowledge into effective measures to combat human diseases pose great challenges for the biomedical science community. Clinical studies frequently reveal gaps in understanding the mechanisms of diseases, but there is a need to improve the linkages back to basic research to fill these gaps. Accumulating evidence attests that mounting barriers between the bench scientists, drug developers and clinical researches may eventually impede progress

in innovative diagnostic and therapeutic methods and drugs. Such situation spurred the paradigm shift in the biomedical research creating the translational research field in the 21<sup>st</sup> century. Through the two-way activities, often called as “bench to bedside” and “bedside to bench”, the biomedical community takes a focused point on streamlining the process of guiding scientific discoveries through the early phases of development into technologies that can be applied to human health.

The essence of this enterprise “translational research” is to pursue many parallel integrations between pertinent information derived from the basic sciences on one hand, and clinical research and practice on the other, by identifying and assessing disease biomarkers and drug-targets, developing and optimising the use of new drugs, and conducting preclinical, clinical trials and post-launch follow up, in order to eventually provide targeted and, if possible, rational patient care.

The described “gap” had detrimental consequences both for the academia and the pharmaceutical industry, considering that the tremendous volume of potential drug targets generated by genomics, proteomics and all the other high-throughput technologies was not assimilated effectively. This unacceptably slow rate in developing diagnostics and new drugs has led to the concept of “translational research”. Biomedical research agencies worldwide have recognised the pressing need for a robust, bidirectional flow of information between basic and translational scientists. Moreover, they realised that science and innovation have become too complex. Thus, they are aiming at developing a new culture in the form of large, multidisciplinary groups that include both basic scientists and clinicians, but also bioinformaticians, statisticians, engineers and industry experts, having as a common objective the translation of the remarkable scientific innovations that we have witnessed during the last years into health gains for society.

The development of translational research does not entail simple reorganisation of traditional clinical research under a new name. It also involves key investments in training, research and infrastructure to help

researchers close the gap and break down barriers in the transformation of basic-science breakthroughs into clinical applications.

Today, the efforts to facilitate the translational research are gaining strength worldwide. The largest world funding agencies in medical research are pooling resources to support the development of translational research capacities. In the United States, the Clinical and Translational Science Awards (CTSA) Consortium, launched in 2006, supports clinical and translational research by providing access to research resources developed by the CTSA, government sponsored research communities, and government agencies. In the US, the National Institute for Health (NIH) has established sixteen Biomedical Research Units linking hospitals and academic centres to undertake translational clinical research in the priority areas of high disease burden and clinical need. Such incentives prompt new initiatives at the institution level.

Over the last decade many world leading universities established specialised translational research centres. In parallel to these new institutional arrangements, large efforts are directed towards the development of a new discipline of translational medicine. This triggers a surge in interest in new master programmes in clinical and translational science. Through such programmes, basic researchers gain understanding of how physicians think about their patient’s problems, and physicians learn techniques for investigating clinical observations in the laboratory. As a consequence, a growing number of well-trained translational investigators are poised to emerge. The new collaborative trends between the private biotechnology companies, public research institutions and universities, attest for the potentially high economic value and social benefits of the translational medicine enterprise. \$500 million for the establishment of Translational Centres across the country are invested by the NIH in the US.

The development of the pan-European EATRIS-initiative, together with other biomedically oriented ESFRI RIs, reflect the serious efforts all over Europe to overcome

obstacles and solve globally and effectively the same vexing problems affecting biomedical research in the rest of the world, such as fragmentation in disciplines, redundancy in activities, gaps in critical infrastructures, inconsistency of standards and guidelines, and incompatible legal and ethical frameworks.

To further foster the European position in biomedical research, other ESFRI initiatives such as EU-OPENSOURCE began to negotiate with EATRIS for synergies employing new models to test new drugs and verify novel therapeutic strategies in disease areas that have a high medical and economic burden and that are of particular relevance for European Member States: cancer, metabolic diseases, neurological disorders, cardiovascular diseases, and infectious diseases. Further clustering and collaboration of BMS infrastructures are encouraged to optimally use European emerging resources.

### Disease Models

In the post-genomic era, in which genes and genomic organisation of human and other genomes were identified, there is a huge demand to attribute the function of individual genes in their complex networks. To accomplish this tremendous task new European RIs were established to facilitate and speed up the discovery of molecular mechanisms of diseases and health. The knowledge of function of all individual genes is crucial for the future of molecular medicine and the development of new diagnosis and therapies.

Related genetic resources are particularly addressed by EMBRC whereas mouse models are the focus of INFRAFRONTIER. Furthermore BMS TWG identified the need for a RI for microorganisms. All these biological resources have several features in common that makes proper coordination across Research Infrastructures obvious. Some of the infrastructures create a virtual meta-infrastructure for certain key problems. For instance ERINHA, BBMRI and the proposed infrastructure for microorganisms will jointly provide a unique framework to investigate pathogen-host interactions and will help Europe to efficiently respond to emerging pandemics. BBMRI, EATRIS and ECRIN will become the key infrastructures

for biomarker discovery and development thereby essentially contributing to the advancement of personalised medicine and to improve efficacy in drug development.

Although non-mammalian models have provided valuable knowledge on basic gene function, the mouse that is genetically very close to humans is ideal to model physiologic functions and diseases of humans, and to test new drugs and treatment strategies.

### High Security Laboratories

In the context of the emergence and re-emergence of human infectious diseases involving highly pathogenic microorganisms, there is a crucial need for Europe to be well prepared to face any pandemic threat. Highly pathogenic microorganisms are characterised by a high mortality rate induction, the unavailability of prophylactic or therapeutic means and easy human to human transmission. All infectious microorganisms are classified by risk group according to pathogenicity, modes of transmission and host range of the organism. The most highly infectious pathogens are classified as risk group 4. To protect environment from spread and to protect scientists from infection, these microorganisms must be handled and stored in Biosafety Level 4 (BSL4) facilities.

When a risk group 4 pathogenic infection of a patient or the presence in the environment is suspected, it is essential that diagnosis and confirmation of diagnosis are performed quickly to ensure proper monitoring of the patient and to mount an effective response to prevent a pandemic or bioterrorist attack. Proper BSL4 facilities are essential to conduct and confirm diagnosis, to carry out research for the development of new diagnosis tools, prophylactic and therapeutic interventions, to ensure correct biological resource management and to facilitate education and training.

At present, all risk group 4 pathogens are viruses. However most of the international experts predict that in a very near future some bacteria strains will join this category. In this context, dedicated areas have to be built and equipped, specific procedures have to be developed and bacteriologists have to be trained.

The research areas of main concerns for this field of science are the development of new diagnosis tools, new prophylactic and new therapeutic means. This research spans from very basic to very finalised, encompassing preindustrial and preclinical tests and translational research all of which involve actors from public and private areas. In the domain of preclinical tests, the availability of animal models is of main importance until efficient alternative models, for example biomarkers, have been developed.

A biological resources bank containing environmental, animal and human samples as well as isolated microorganism strains is crucial for research and diagnosis activities. Further education and training in areas of microbiology, the biosafety and biosecurity fields are also important components for high security laboratories development.

All these aspects will be developed at the European scale in ERINHA, a pan-European BSL4 infrastructure. ERINHA will also develop close integrating activities with, in the first instance, BBMRI, ECRIN and EATRIS to protect against human infectious diseases.

### **Biomedical engineering and related areas**

Biomedical engineering has been a rapidly progressing area at a broader cross-section of Life Sciences, engineering and material sciences. From the prosthetic devices to engineered tissues and to drug monitoring systems, from blood pressure devices to PET scans, the biomedical technologies serve to large degree not only the academic research field but also the public directly. Biomaterials stand as a potential solution not only for medical applications but also many other biotechnological applications including sensors that would help monitoring and cleaning biohazards. Tissue engineering is a young field which could ultimately unite synthetic and "natural" cells on suitable scaffolds into new organs etc. Biomechanics and advances in mechatronics will have a potential role in supporting the needs and health of the aging population including artificial replacement of bone, cartilage and other structural tissues. Brain computer interface and interfaces between nerves and

prosthetic devices and similar applications of the future can become means to increase the quality of life, finding applications from the usage in cases of disability to even industrial production lines. Accordingly, state of the art RIs are needed to organise, stimulate and amalgamate cross disciplinary efforts into world leading scientific and technological leaps for Europe.

As a field, it has been welcomed into European landscape rather quietly. As early as the FP4, there have been cases like BIOMED2 with collaborative (about 50) projects in this field. Starting with FP5 the focus has been somehow missed more diffused and fragmented topics appeared throughout FP6. Yet according to a recent report on biomedical engineering and eHealth in Europe such as personal (wearable and implantable) eHealth systems, assistive and rehabilitation technologies, micro- and nanosystems, and bio-inspired information technologies were addressed in the Information Society Technologies Programme; neurosciences research, radiotherapy and medical imaging were funded as part of the Life Sciences, Genomics, and Biotechnology for Health Programme; and biosensors in the Nanotechnologies Programme.

The strength of the biomedical area lies in the fact that it is also one of the better examples of fusion of innovation, education and research. In this respect, a curriculum on biomedical engineering has already been established to the internet for European universities under a project, European Virtual Campus for Biomedical Engineering (EVICAB), with an aim of forming synergies to facilitate the implementation of the European Higher Education Area (EHEA) in the field of medical and biological engineering and sciences for the benefit of the universities, the students and last but not least the European people. Thus, the education scope of biomedical area has also been made available as a distributed system. The small scale innovative throughputs of this area can be achieved in various levels of BMS research scope. The amalgamation of SMEs and industry into this innovation-research and education triangle is extremely feasible in the biomedical field. In this scope, the FP7 project SM-BIO-POWER has targeted to

empower biomedical engineering SMEs to participate in EU research.

### 3.1.4 Future Perspectives

ESFRI BMS identified 3 new proposals in key scientific areas of the BMS landscape and has recommended them to ESFRI for inclusion in the ESFRI Roadmap 2010. There are, however, other important scientific fields that are still not sufficiently promoted and developed, and which will be required for the progress of the European Research Infrastructure Landscape and its positive impact on the ERA. These research areas include, for example, synthetic biology, biological energy production and agricultural research, all of which will play a major role in the future. The BMS TWG will monitor their development for the next edition of the ESFRI Roadmap in order to support the ESFRI incubator role.

#### **Towards the successful development of a European-wide integrated knowledge economy**

The global research and economic state now facing the first wave of BMS RIs is one that has dramatically altered since the first 6 projects entered the ESFRI Preparatory Phase in 2007, and is one that is continually and rapidly transforming. The globalisation of research activities, with the emergence of new knowledge production countries such as China and India, requires renewed and coordinated efforts if Europe is to position itself as a centre of competitive excellence with a thriving knowledge economy embedded in an innovation ecosystem. A robust pan-European integrated biomedical research arena will enhance the competitiveness of European biotechnology, pharmaceutical and healthcare industries, driving economic performance and sustainability. Europe and the rest of the world face a series of major societal challenges that call for urgent solutions. Most of these Grand Challenges such as global warming, tightening supplies of energy, water and food, an ageing population, public health, pandemics, and security can only be addressed in a globally coordinated manner. Confronting these challenges and alleviating the impact of future challenges requires mobilisation of European science, technology, research,

and innovation resources in a coordinated manner.

ERIL, which is emerging through implementation of the goals of the European Research Area, provides the framework for expanding Europe's knowledge economy and is core to addressing global Grand Challenges. To attract the best researchers and foster an innovation environment, this integrated RI network must be world-class in science and technological competencies, internationally accessible, and have in place robust and appropriate governance structures. Establishing high quality RIs across Europe will generate a European biomedical research arena, providing the framework for stimulating growth in a European-wide knowledge triangle of excellent scientific research, education and training, and open innovation. The distributed nature of RIs envisioned in many of the BMS projects offer a unique opportunity to create networks of centres of excellence throughout Europe that foster a dynamic innovation environment through cross-border collaboration in researcher mobility, scientific disciplines, ideas, and technology.

As the current BMS RIs progress through the ESFRI process, Europe is very well positioned to respond to global challenges by fostering excellence in research and development in a broad spectrum of relevant fields. However, Europe's competitive position is strongly dependent on how well Europe is able to collaborate at the global level. Therefore Europe must not only concentrate on the implementation of RIs in Europe but must ensure proper global integration. This global integration process requires support on the science policy level and appropriate funding mechanisms.

The absolute scientific need for developing ERIL consisting of integrated, functioning, and sustainable RIs is clearly demonstrated by the enthusiasm of researchers, institutions, and Member States to join the Preparatory Phase of ESFRI BMS Research Infrastructure initiatives. Unified and focussed approaches to seek resolutions to barriers hindering European-wide research efforts have resulted in the development of the Community legal framework for a European Research Infrastructure

Consortium. The ERIC framework, in conferring distributed RIs with legal responsibility and identifying the basic **governance structures** necessary for successful development of RIs, is the first step in addressing complex issues facing facilities operated and governed by multiple EU Member States. Further coordinated efforts are needed to drive a unified decision making process that addresses trans-national obstacles such as access to facilities, data/sample storage, data management and financial/operational costs. Secure financial sustainability for these distributed infrastructures will require a reassessment of national policies to ensure that national science policy is cognisant of European interests and to ensure that pan-European networks are robust and sustainable. The contribution of individual Member States to long-term investment in BMS infrastructures can only be secured if there is a clear impact of BMS RI initiatives on the knowledge triangle. To this end, robust and meaningful mechanisms must be put in place to measure the value and impact of BMS RIs.

### Access

The BMS RIs offer European researchers' access to a range of facilities and the latest technologies advances regardless their geographic location. Access to RIs is crucial to researchers working at the forefront of science to allow them to remain internationally competitive. The RIs must therefore implement mechanisms to ensure their optimal use and operation so that they can be accessed effectively and provide an essential service to the research community. Further development of the European Portal on Research Infrastructures Database, currently hosted at <http://www.riportal.eu>, which serves to identifying facilities, resources and related services offered by RIs in Europe would be of interest for potential users, policy makers and other stakeholders.

An open access and open competition policy throughout Europe would allow national facilities to benefit from the flow and exchange of man power and ideas, and maintain and improve the quality of European research. It would maximise the networking between the best researchers, speed up progress and avoid waste of

resources, allowing maximal profit of human and material resources in Europe. Historically, EU Framework Programmes have provided some support for trans-national access through financing travel, subsistence and operational costs linked to the services for users from countries outside those operating the infrastructures. These programmes helped to optimise the use of RIs on a European scale, and to progress towards a single "market" of services.

ESFRI BMS RIs will need to develop open and trans-national access policies and it is likely that one size will not fit all. For instance, access to human biological samples and medical data has to be compliant with a series of regulations that vary from country to country, and depends on informed consent given by the sample donor and on approval by research ethics committees.

Each infrastructure will have to identify the share between national users, other European users, or non-European users, and how to fund these respective categories. It is suggested here that future Framework Programmes should significantly reinforce support for European users. Also, it is felt that the overarching principle for access to RIs should be a transparent assessment procedure, where applications for facility time, resources and services are submitted and peer-reviewed using agreed and publicly available evaluation criteria. The evaluation criteria should include: scientific quality and innovation of the plan; instrumental and/or methodological relevance; track record of applicant and/or research team; feasibility of the plan; impact on training of researchers. It will be essential that RIs work together to align their access policies, assessment criteria, and review of applications.

### Data storage and management

The generation of data from Life Sciences continues to increase at gargantuan rates. The knowledge generated by the data is also fast developing: it is estimated that scientific papers are now published at a rate of five per minute. Creative measures, instruments and policies must be developed to enable, support, and facilitate the mobilisation, sharing, and exchange of data and knowledge so that is available to the



community, is useful and truly accessible to all, and allows full intellectual and commercial exploitation.

The BMS RIs have a major role to play in capturing the returns on that knowledge, as incubators of knowledge creation and development. This return can be achieved by maximising the potential for data exchange between RIs and the lifespan of the data and knowledge generated and facilitating the standardisation of common practices. It is critical that this knowledge is accessible to the scientific community across an integrated platform. As globalisation accelerates, such an integrated approach to the management of data and knowledge will improve the connectivity between scientific and technological advances and an innovation environment that is necessary for the creation of growth and wealth.

Current rules of intellectual property (IP) protection favour vast amounts of data, information and knowledge to be held proprietary. While IP rights are necessary as an incentive for innovation, in reality full exploitation of this knowledge is not possible as the scale of the data generated often exceeds the human capacity, resources and time scales to be exploited by their own producers. There is, therefore, a substantial amount of knowledge and other intellectual assets that are not core business and could be shared. Funding bodies and journals are favouring more and more the release of data to maximise the value of the information and to accelerate scientific progress, particularly in pre-competitive research. Early data release, i.e. pre-publication, is being encouraged and the citation of unique data identifiers is developing as an appropriate mechanism to give credit to data producers in a similar way to publication credits. Through the operation of an integrated platform for the management of data and knowledge, the BMS RIs could provide the foundation for an agreed set of data management principles and policies that facilitate the deposition, retention, and exchange of assets, while securing their lifespan and long-term sustainability.

The fast rate of scientific and technological advancement in the Life Sciences, the volume, complexity and heterogeneity of the

knowledge that is generated, and the need for its integration and interoperability, all represent a real challenge to effectively harvesting the full benefits of the existing knowledge base. The BMS RIs are set to address precisely this challenge. Technological solutions will need to be developed and/or deployed to generate this integration and interoperability and to face this "data deluge". It is crucial that BMS RIs benefit fully from e-infrastructures services such as Géant (for global connectivity), EGI (for Grid computing), PRACE (for High-Performance Computing), and that no gap remains between BMS infrastructures and these service providers. This would be an important step towards the realisation of ERIL.

### Impact

The BMS RIs enable research to seek insight into the basic processes of life leading to the development of more effective measures for improvement of life and, thus, touch the society at its very core, health and wellbeing, a sustainable food supply, and a protected environment for all. This compares to the building of the large physical instruments with the goal to seek insight into the structure of matter leading to the development of new materials for new products.

BMS RIs will first directly generate knowledge by giving access to key technologies and competences and will thus improve responsiveness of research to the needs of the global economy. They will facilitate knowledge sharing as well as training. The new RIs will underpin national and European science investments and play a key role in attracting the next generation into careers in science, technology and engineering, and in expanding the current skills base in scientific and technological problem solving. The new RIs will have a cultural and symbolic impact, through visibility at regional, national, European and international levels. The RIs will contribute to and promote harmonisation of the scientific landscape in Europe. Through setting of standards, harmonised procedures and/or quality assurance, the BMS RIs are likely to become drivers of these practices across their scientific communities.

RIs will also stimulate innovation by generating new technologies that lead to new goods and services, and will contribute to building industrial capacity by creating new firms and attracting inward investment. This can be illustrated by technologies such as imaging or NMR instrumentation, for which the new BMS RIs, through generation of the knowledge triangle, will foster technology developments. The long-term impact of BMS RI generated technological developments will filter down to improve tools in every university and research centre as in the domain of Life Sciences, more than any other field of science, there is a continuum between large-scale technological improvements and advances in small laboratory equipment for the basic science researcher.

In contrast to the single-sited infrastructures of the physical sciences, the BMS RIs are of a distributed nature. BMS RIs constitute a singular Research Infrastructure but its research facilities have multiple sites. The BMS RIs are therefore very distinctive and require that specific measures of progress and impact are developed. There is an opportunity for the recently created ESFRI Working Group on Evaluation (WGE) to draw on ESFRI BMS expertise in this aspect. The ESFRI BMS TWG would welcome to interact with and contribute to WGE work of ensuring that optimised procedures are established for evaluation.

The BMS scientific landscape is vast and encompasses basic biological sciences, biological resources and production systems for food and non-food applications, and the medical sciences. As science evolves and the BMS scientific landscape expands the likelihood of new RIs to emerge in areas sitting at the boundaries of other ESFRI TWGs increases. The BMS TWG favours this development and the interaction with other TWGs to guarantee that there are no gaps in the ERIL and that resources are maximised. The new RI ANAEE, recommended to ESFRI in this report, is a primary example of an infrastructure operating at the interface of two TWGs, BMS and ENV (see Chapter 5 "Evaluation of new proposals"). There has been a substantial interaction between BMS and ENV during the assessment of this RI as BMS relied on the complementary scientific

expertise provided by this TWG. ESFRI BMS envisions this process to continue during the monitoring and assessment of the RI, should ANAEE be successful in getting financial support from the EC for a Preparatory Phase project. BMS will ensure that its interactions with ENV are fostered for this purpose.

Appropriate mechanisms to measure the progress and impact of BMS RIs on the science, on the communities they serve, and on society should be established. However, we can already foresee that new RIs will bring numerous benefits for Europe. The new BMS RIs are poised to become a structuring element of the broader European research and innovation ecosystem, stimulating the progress and competitiveness of Europe and driving economic growth. This new research landscape will be core to addressing the Grand Challenges of the 21<sup>st</sup> century: global warming, tightening supplies of energy, water and food, an ageing population, public health, pandemics, and security.

#### **Financial framework for construction and sustainability**

Initiation of the ESFRI process focussed thinking on national gaps in RIs, which led to a number of Member States developing national roadmaps and prioritising involvement in BMS RI initiatives. However, Europe's economic outlook is very different to that of 2006. The global economic downturn has forced Member States to take an insular view of the best output for scarce national resources. With scarce resources for additional major investment in research and development, Europe is now focussing on new approaches to increase the efficacy and impact of national public funds in strategic areas by enhancing cooperation between Member States. The emerging BMS landscape will provide the framework for collaborative research programmes, such as those of the Joint Programming Initiative, which is a voluntary, bottom-up approach that aims to better address major societal challenges (see Chapter 2.1.4 "Increased relevance of RIs in the Life Sciences area"). This and future European cooperative research schemes will be possible in the context of functioning, accessible and cutting-edge RIs. Collaborative research programmes are not

sufficient to fund construction and operation of these networked RIs, however. Indeed, implementation of the first wave of BMS RIs is proving to be a rather slower process than that envisioned at the outset of ESFRI. This is in one part due to the funding mechanism of ESFRI; commitment to fund and long-term sustainability of the RIs relies on the interests and funding priorities of individual Member States. While a number of Member States have committed significant national funding to construction of BMS RIs that received high priority on their national agendas, there is a concern that the implementation phase of some projects will stall, not due to national support but due to a lack of national commitment.

The distributed nature of many of the BMS initiatives offers the advantage that the initial construction costs to implement these RI initiatives will be much lower than that of other fields of science where a new and operational infrastructure is required upfront. This may allow some BMS RIs to initiate their construction and implementation sooner, in a scalable and progressive manner. However, sustainable operation of these RIs necessitates a commitment from individual Member States to long-term funding prioritisation. With reducing national budgets and increasing constraints on those resources, it is clear that the current ESFRI funding mechanism needs complementary mechanisms to address the operational needs, strategic direction and long-term sustainability of these important infrastructures.

The welcome publication of the Strategy Paper on the emerging European Biological and Medical Sciences Research Infrastructures invites the European Parliament and the Council of the European Union to influence key decision making processes to support implementation of BMS RIs. In this Paper it is asked that the Parliament and Council develop a European level mechanism for sustainable support of these infrastructures, explore opportunities for tailored funding instruments to ensure construction, operation and access, and engage with BMS RIs to secure a harmonised and sustainable implementation process tailored to the specific needs of each infrastructure. At this stage of the BMS ESFRI Roadmap, it is imperative that Life

Sciences researchers organise into one coherent voice to raise awareness nationally, in Europe and internationally, of the vital role of basic and applied Life Sciences research in driving a knowledge-based society capable of addressing and tackling major societal challenges.

### **Integration of Central and Eastern European Countries in the ERIL**

The accession of ten new members to the European Union in May 2004 was one of the most significant developments in the history of European integration. The incorporation of Central and Eastern European Countries (CEECs) continued the process of progressive enlargement of the Union. Today, it still represents a challenge for both, existing members and the CEECs. Conceptualisation of European academic and research area needs to be based on involvement of all Member States, facilitating a progressive, but solid, integration.

The CEECs are the Czech Republic, Cyprus, Estonia, Hungary, Latvia, Lithuania, Malta, Poland, Slovakia, and Slovenia. While the economies of the new members seem relatively small, the dynamics of growth and their scientific potential, in terms of their strong academic community and worldwide leading science institutes promise to enhance the scientific landscape and to provide a key impulse to future economic development in Europe.

There is a strong interest in CEECs to enhance their scientific cooperation with the EU-15. The ESFRI BMS RIs have a key role to play to ensure that the CEECs are integrated in a timely manner so that they build on the opportunities that the BMS RIs have to offer and prepare the ground for participation. While it is acknowledged that this poses an additional challenge to the RIs, there is a strong commitment in each of them to close the cultural, methodological, and structural gaps between the scientific communities in Eastern and Western Europe, and to integrate them into the broader European and world community of scientists. Cooperation between the ESFRI BMS RIs and the CEECs should take particular account of the special features, priorities, and needs of these countries. The CEECs, in turn, have the commitment to

effectively respond to the significant opportunities for cooperation and mutual benefit offered by the RIs.

The mission of ESFRI BMS TWG is to foresee the needs within its scientific landscape that will allow the development of the most competitive society in the future. BMS believes that the conceptualisation of European academic and research area needs to be based on a more even distribution and involvement of all Member States allowing, when necessary, a progressive but solid integration. The current organisation of distributed Research Infrastructures provides an excellent opportunity for integration of European academic and research area in terms of scientific and professional excellence, knowledge transfer, mobility of human resources, and regional development. Such organisation is needed both due to the nature of biomedical research originating from the diversity and distribution of subjects under investigation as well as due to the societal needs of access to such infrastructures. Despite of these advantages, BMS still observes that CEEC Member States are lagging behind in commitments to actively join the established RIs in the BMS field.

The BMS TWG is aware of the numerous initiatives, being undertaken at national and EU levels, to ensure greater coherence and synergy in the creation of a globally competitive knowledge based and innovative Europe. Yet there is a need to appeal again for an action plan to address the active participation of CEEC Member States in the BMS RIs. Only such action will allow the development of the European human potential and protect the ERIL from brain drain and regional unbalances.

### **Engaging with the global research platform**

Scientific research has always been an international effort. However, the globalisation phenomenon and its economic, social and political dimensions, is accelerating and with it, the globalisation of research and technology. It is now increasingly acknowledged that international growth is driven by increasing science and technology capacity in economies around the world. Investments in science and

technology are proving to generate new jobs, attract private investment and promote economic prosperity, and are at the core to addressing national as well as global challenges. Revolutionary advances in information and communication technologies are providing opportunities for scientific exchange and for increased global science and technology capacity. In parallel, new scientific and technological powers are fast emerging and attracting new investments. This creates new opportunities for Europe and the world. The BMS RIs should seek to establish and renew international collaborations and to construct solid, long-lasting partnerships that will secure a sustained and effective progress in critical areas, enhance the mobility of researchers and promote the efficient sharing of resources. The process of engaging with partners outside Europe should be developed in a way so that it complements national and EU policies and efforts to address these challenges and other global research activities. The national priorities for international cooperation should serve as vehicles to reach out to RIs in developed, emergent and developing countries hosting equivalent resources and capacity, or hosting very specific yet essential resources from which BMS RIs may benefit. The international partnerships developed by the RIs may, in turn, have an influence in the development and implementation of national policies.

### **Emerging BMS fields and future challenges in biotechnology**

The inception of ESFRI BMS initiatives 4 years ago has empowered Life Sciences researchers to address high priority gaps in RIs where critical requirements were identified. The 10 projects currently on the ESFRI Roadmap address the broad spectrum of Life Sciences research requirements, providing a framework to conduct excellent scientific research, from basic biological to translational activities, underpinned by advanced bioinformatics and imaging technologies. Life Sciences research is dynamic, and there is a requirement to now fill remaining gaps in terms of RI needs that will enable researchers address global grand challenges, face future challenges and advance science and technology development.

A welcome proposal to this update of the BMS TWG Report is the development of an interconnected European RI for systems biology. Another emerging field challenging scientific concepts is that of **synthetic biology**, in which ground-breaking research has already enabled scientists to create a synthetic cell controlled by designed synthetic DNA. By applying the principles of engineering to the biosciences, synthetic biology can explore the design and construction of new biological parts and systems, and the redesign of existing biological systems to deliver novel functions that do not exist in nature. Potential applications of the field are diverse and promise to offer societal, environmental and medical benefits: vaccines and pharmaceutical drugs; biosensors; bioremediation; cell factories; biomaterials; gene therapy; biofuels; food ingredients. Intrinsic to synthetic biology is the aim to increase our understanding of the origin and function of biological systems. Both the scientific community and funding organisations agree that these applications can only be developed successfully and to their full potential if the ethical and societal issues associated to them are considered alongside, and are resolved. Synthetic biology is a rapidly developing field, highly interdisciplinary in nature, which is already impacting hugely on Life Sciences research and will continue to do so in the future. ESFRI BMS will explore whether this field can be integrated into the existing BMS RI Landscape

**Agriculture, food security and climate change** are highly interrelated societal challenges where resources must be focused to protect the environment, food production and thus human health and wellbeing. The critical global impact that human activities and the progress of civilisation is now being witnessed; scientific and engineering solutions are needed to address the problems affecting biosphere productivity, food production and to determine the impact of climatic changes and emerging chemical and biological concerns. In an era of dramatic changes in climate, land use, and other human activities, understanding the responses of the biosphere to human drivers of environmental change is both an intellectual grand challenge and a practical necessity.

An infrastructure for analysis of ecosystems should aim at developing a coordinated set of experimental platforms to analyse and predict the responses of ecosystems to environmental changes and to engineer management techniques to deal with these changes. This will be achieved by setting-up a distributed and coordinated network of well equipped state of the art experimental platforms associated with analytical and modelling platforms. The analysis of ecosystems could be driven by the currently proposed BMS Infrastructure for Analysis and Experimentation on Ecosystems (ANAE). This initiative aims to set-up a distributed and coordinated network of experimental platforms that will be associated with analytical and modelling platforms and linked to networks of instrumented observation sites. In this manner, ANAE will bridge the existing research gap between monitoring and observational and functional experimental approaches, fully integrated towards modelling and prediction.

**Bioenergy**, the use of biological feedstocks as sources of energy, is a relatively new area of science but one that is gaining strength across Europe. Renewable energy technologies are required to meet targets for reductions in greenhouse gas emissions; bioenergy can play an important role in this if the potential for greater biofuel production across Europe is realised. Current challenges in bioenergy include the development of new feedstocks and/or the improvement of existing ones to enable growth of biomass crops on marginal land, with minimal water and fertiliser input, increased photosynthetic conversion, and better disease resistance. Bioenergy research requires the skills of scientists working in plant and crop science, microbiology, chemistry, enzymology, modelling, process engineering, environmental science, agronomy and social science. Many of these areas, such as crop science, are well-developed across Europe and the skills required already exist. Many researchers in these areas are starting to work on aspects of bioenergy but would not regard themselves as bioenergy scientists. Greater training opportunities could increase the number of younger researchers moving into bioenergy research at an early stage in their career. Developing an integrated

bioenergy community across Europe will be the key to maximising potential collaborations and ensuring a coordinated approach to bioenergy research.

**Bioprocess engineering** is developing rapidly to satisfy the pressing demands for biofuels and bioproducts. Bioprocess engineering translates life-science discoveries into practical products, processes, or systems. Bioprocess technology makes bioproducts available at large scales, at low cost, and with acceptable purity. This is an area with enormous potential as biofuels and bioproducts are demonstrating their capacity to foster the growth of rural and forestry economies and of new industries, such as biorefineries to make fuels and chemicals. The range of bioproducts includes bioethanol, biodiesel, biohydrogen for biofuels, biopolymers and the renewable chemicals propenediol and lactic acid.

Biological processes offer alternative ways to remove toxic pollutants from industrial and municipal wastes. **Bioremediation** continues to develop as a solution with lower cost implications, compared with other types of technology, for cleaning up the environment. Bacterial bioleaching, i.e. bacteria that extract metals from mine wastes, is a growing sector of the mining industry and several developing countries are already playing a key role in this area.

BMS TWG will explore how best to develop and integrate the above fields into its scientific landscape.

An area that impacts many efforts on understanding biology and pathobiology is the role of mechanical load at the cellular level as well as at the organism level. To enforce the area of **biomechanics** efforts are in need both at the level of science and of the supporting infrastructure. There are multiple important general questions in this area to be addressed including how mechanical loads alter cell and matrix dimensions and how do mechanical loads alter gene and protein expressions in different cell types. In addition, many specific questions within multiple biomedical research areas are important to solve for medical application and as such mechanobiology merges the older science

of mechanics with the newer and emerging disciplines of molecular biology and genetics. This area will therefore provide important tools to develop the technology for implants (cell and devices) which may reduce organ function impairment at any level in any organ of the human body.

A major impact of the emerging BMS landscape will be the **technology innovation framework** that will develop and advance as the scientific and technological competencies of these integrated facilities grow. Advances in biomedical engineering will emerge from development of sustainable new materials for medicine and energy; advances in tissue engineering and organ generation will be realised as understanding of complex biological and cellular process continues; and medical interventions will benefit from increased understanding of the field of biomechanics. Advances in bioprocessing engineering for biofuels and bioproducts will benefit from further optimisation of current technologies and the development of new methods to reduce environmental impact. BMS TWG will investigate the further requirements for technology innovation across the ERIL. The technology innovation framework will be instrumental in realising solutions to global Grand Challenges, developing technologies to combat climate change, address the need for a variety of renewable energy sources, protect against pandemics and address the balance of biosphere productivity.

### Integrating efforts

The integration of different types of collections and biological resources will enable research on highly complex topics such as long-term effects of environmental changes on living organisms and human health. All of the scientific fields create resources that are necessarily interacting. Ascribing gene functions and elucidating complex gene networks in mouse models through INFRAFRONTIER will translate into clinical research through collaborating efforts with BBMRI. As pathobiology-related materials identified in the mouse are correlated with human samples collected through BBMRI, further analyses of human disease will demand manipulation of mouse models to verify pathological mechanisms of disease. INFRAFRONTIER and BBMRI, through advancing understanding of

disease, will integrate with EATRIS and ECRIN and Euro-Biolmaging in translational and clinical medicine applications of new drug targets and biomarkers of disease. Thus, research disciplines focusing on human health draw on the know-how of INFRAFRONTIER, BBMRI, ECRIN, EATRIS and Euro-Biolmaging, and will further integrate with EU-OPENSREEN, INSTRUCT, EMBRC and ERINHA (high pathogenic organisms) and the proposed facility MIRRI (microbial resources) to create a full picture of cellular and biological process in health and disease. As the change of the climate, food production and quality, alteration in biodiversity, spread of pathogens, and needs for new energy resources can also directly or indirectly effect the human wellbeing and health the biological resources and biotechnology platforms must be effectively combined.

For instance, the proposed infrastructure MIRRI will complement ESFRI BMS initiatives such as EMBRC (focusing on marine biodiversity, “blue” biotechnology), BBMRI (focusing on primary material of human origin, “red” biotechnology) and ERINHA (high pathogenic organisms) by focusing on green and white/grey biotechnology sectors. These areas would cover food security in its largest sense as well as support for the agricultural and industrial biotechnology sector. MIRRI will be the link between the collection community, users of microorganisms, policy makers and research programmes. Microbial resource collections can also be exploited for global research, cross-cutting the agricultural, food, healthcare and biotechnological sectors providing a basis for a bioeconomy. More and more natural resource alternatives are being found using cells as factories e.g. biofuels, drugs, functional foods and nutraceuticals. This has been stressed in the OECD work towards the establishment of a Global Biological Resource Centre Network (GBRCN) in providing key resources for the development of microbiological and human health-based industries leading to economic development ([www.gbrcn.org](http://www.gbrcn.org); [www.gbrcn-human.org](http://www.gbrcn-human.org)).

Integrating efforts across research disciplines will allow scientists to apply their skills and knowledge in one research field to different and emerging fields, creating more

training and career opportunities. Examples of interdisciplinary research fields include synthetic biology and bioenergy, which require the skills of engineers, chemists, biologists, physicists, social scientists and many others working together.

### **3.2 Identified needs for new generations of Life Sciences RIs**

An in-depth analysis of the needs of the potential user scientific community(ies) within the next 10-20 years is the challenge that has to be mastered when identifying the requests for future Research Infrastructures in the Life Sciences sector.

In this context it has to be distinguished between (i) the applied methodologies and tools and (ii) the specific research areas integrated in the 3 distinct pillars of research in the Life Sciences – “Biological Sciences”, “Biological Resources and Production Systems” and “Medical Sciences” - which are reflected by the BMS TWG scope (see Chapter 2.2 “BMS Thematic Working Group’s scope”).

As a result of the painstaking requirements analysis the following 3 fields of research were identified revealing the needs for the next generation Research Infrastructures in the section of Biological and Medical Sciences. Following the identified gaps in the BMS Report 2008, ESFRI launched a call for new projects to be considered for the update of the ESFRI Roadmap (see Chapter 5 “Evaluation of new Proposals”).

#### **3.2.1 Systems Biology**

The main objective of the innovative and promising branch of science, systems biology, is to investigate biological processes on a systems level to understand life processes. This highly interdisciplinary approach analyses the dynamic of life processes relating to all stages: starting with the genome and the proteome up to the cell and its organelles ending in the whole organism or even populations. Systems biology intends to rebuild the organisms based on the newly identified parts – cells, proteins and genes and their interactions –, and to foresee their behaviour under all conditions. Systems biology has already been identified as need for a new generation

of Life Sciences Research Infrastructures in the BMS Report 2008.

Systems biology combines mathematical modelling with experimental approaches to predict and explain the functional architecture of genomes across the diversity of organisms. Therefore systems biology unites quantitative methods used in molecular biology, biochemistry and chemistry with approaches from engineering technologies and the fields of mathematics and computer sciences (including modelling and simulation) to cope with this task.

In this context completely new insights for biomedical research, agriculture and industry will be generated. Practical advances in healthcare, industrial biotechnology and sustainable food and environmental sectors can be achieved by using systems biology. Even highly complex research areas, such as pharmacology or human/animal/plant physiology can be addressed.

With regard to these aspects it is essential for Europe's science sector to deal with appropriate research institutions, especially in comparison with the United States and Japan, where systems biology has a long standing tradition.

Obviously, there is an urgent need for systems biology RI in Europe and there are already many national initiatives in this area. Numerous European States as well as the EMBL have started to develop this scientific branch. For instance 6 Centres for Integrative Systems Biology (CSIB) were established by the BBSRC in the UK. Four FORSYS-Research Units for systems biology were funded by the German Federal Ministry of Education and Research. Another example is the Netherlands Consortium for Systems Biology (NCSB) that implements systems biology as a powerful scientific approach. The Finish SYSBIO Research Programme also aims to develop research and research environments, national and international networking and researcher training. HepatoSys is a German national project dealing with systems biology of hepatocytes. HepatoSys/Virtual Liver concentrates on a quantitative understanding of complex and dynamic cellular processes in regeneration

as well as detoxification and de-differentiation in human hepatocytes. The encouragement of work in systems biology in Germany was further advanced through the promotional focus of FORSYS allocating the structural and content requirements for work in systems biology and even providing the basis for the creation of educational opportunities.

Although there exist some research consortia on European level, a RI dealing with systems biology has not yet been initiated. Up to now there is no competitive Europe-wide networked research in systems biology. However, there are several renowned research groups in this area field across Europe. For example, EUSYSBIO is a Specific Support Action (SSA) within the 6<sup>th</sup> Research Framework Programme of the European Union. The Yeast Systems Biology Network (YSBN) is a consortium of researchers promoting systems biology with the yeast *Saccharomyces cerevisiae* as a model system. The YSBN project is an EU Collaboration Action (CA) sponsored for three years under the 6<sup>th</sup> Framework Programme that started in 2005 involving 17 academic partners and 2 SMEs. Another example is the European project SYMBIONIC as a SSA aimed at establishing a European-wide initiative in the field of the systems biology of the neuronal cell. The development of a European assistance measure for systems biology, the ERA-Net ERASYSBIO, paves the way for collaborations beyond national borders. In this connection, projects are supported which both expand the science of systems biology and undertake coordinating tasks that support this progress.

In view of all this innovative approaches it is indispensable to fill this gap as soon as possible and to include within a European Research Infrastructure on systems biology relevant activities in related disciplines.

### 3.2.2 Biorepositories – Microorganisms

Biological resources, such as microorganisms and their derivatives, are the essential raw material for the advancement of biotechnology, human health and research and development in the Life Sciences. The ESFRI Roadmap 2008 emphasises the evident need for improved availability of high



quality materials and reagents for the study of species other than humans i.e. animals, plants, bacteria and microorganisms. Most biotechnological sectors will be cross cut and supported by a RI in this specific field of science. This will also improve the knowledge about microbial diversity in the area of food, agriculture and soil fertility required to develop approaches to optimise agricultural and food production. Products derived from microorganisms including drugs, antimicrobials, biopesticides, industrial enzymes and biofuels can be manufactured in best quality under ideal conditions. These optimal managed resources will lead to further discovery in all areas of the Life Sciences including healthcare. Ideally the services and resources will be integrated to bridge the gap between the organism and the provision of innovative solutions and products for green, grey and white biotechnology. In addition to that, it is required to provide coherence in the application of quality standards, homogeneity in data storage and management and sharing the workload to help to release the hidden potential of microorganisms.

A Research Infrastructure initiative in this scientific field will build the European platform for microorganisms within the future GBRCN and enhance already existing European microbial collections linking them to non-European country partners globally. The basis for such a RI in the microbial area was prepared by the OECD Biological Resource Centre Initiative spanning 1999 to 2006 which has proved immensely important in providing best practice and the cornerstones for biological resource networking. The networking of the partners will enable a broader coverage of bioresources and services provided. On European level efforts already been made to harness the impact of collections' networking. For instance the European Culture Collections' Organisation has incubated several European initiatives that have helped to optimise collections as for example, recent European Community Framework Programme projects such as the Common Access to Biological Resources and Information (CABRI), the European Biological Resource Centres Network (EBRCN), and the European Consortium of Microbial Resource Centres (EMbarC). The

EMbarC project has started the process of establishing policy for deposit of microorganisms in microbial resource centres.

European microbial resource collections would be united together with stakeholders (their users, policy makers, potential funders and the plethora of microbial research efforts) by a Research Infrastructure in the scientific area of Biorepositories – Microorganisms aiming at improving access to enhanced quality microbial resources in an appropriate legal framework, thus underpinning and driving Life Sciences research.

### **3.2.3 Green Biotechnology & Biological Sciences**

The continental biospheres are playing an important role on global change of the planet due to their interactions with atmosphere and hydrosphere. Severe manipulations through human activities are also crucial for effects on the environment. Therefore a major challenge for ecologists and agricultural scientists consists in predicting and mitigating the consequences of these changes. For this purpose highly instrumented Ecotrons, analytical and modelling platforms, and data bases are indispensable to cope with the task to analyse, simulate and predict the consequences of global changes on ecosystems. A Research Infrastructure providing the settings for analysis and experimentation on ecosystems and organisms with regard to current and future environmental changes would be the best precondition for a strong, integrated and innovative development in a coordinated way across Europe and beyond.

Integrated experimental facilities have to be developed in Europe to solve the problem of fragmentation of environmental and biodiversity research through a multi-disciplinary approach (biogeochemistry, soil microbiology, atmospheric chemistry, hydrology, agronomy, forestry etc.). It is most important that major ecosystem processes can be analysed simultaneously and to enable studies of interactions and the relation of ecosystem functions and services to biodiversity.

In recent years some progress occurred on national level (e.g. in France, Spain, Germany, Norway or the UK) in terms of developing biodiversity-exploratory infrastructures and well-instrumented platforms for networking, analysing, monitoring and modelling. Beyond that, great efforts were made in the scientific field "Green Biotechnology & Biological Sciences" on European level. For example, the Design Project EXPEER will set up a common framework for improving the quality and performance of experimental platforms and sites in a durable and sustainable manner.

The advantage of a European Research Infrastructure in this field is the possibility to regulate a distributed and coordinated network of state of the art *in situ* and *in vitro* experimental platforms equipped with the latest instrumentation. These platforms will be associated with analytical and modelling platforms and in addition will be also linked to networks of instrumented observation sites. With this European Research Infrastructure the further development of ecosystem science into modern systems biology will be possible by (i) generating and testing hypotheses and (ii) giving prognosis as to ecosystems services under various future environmental and socio-economic scenarios.

### 3.3 Processes beyond ESFRI

In Europe there are additional developments identified besides ESFRI dealing with the improvement of circumstances to successfully realise pan-European Research Infrastructures in the Biological and Medical Sciences. In the following chapter these platforms representing European stakeholders, committees or organisations formulate their key messages, recommendations and suggestions that they see in particular in the field of Biological and Medical Sciences.

#### 3.3.1 Survey on Research Infrastructures in the area of agri-food research<sup>8</sup>

The main objectives of the Standing Committee on Agricultural Research Collaborative Working Group (SCAR CWG) were to strengthen the strategic development of European Research Infrastructures in the agri-food research domain and to foster and improve the collaboration between the actors from Member States and Associated Countries in this area.

SCAR CWG's survey, which was carried out in 2009 and finalised in February 2010, identified those research domains for which shared and pan-European RIs are needed and crucial for a highly competitive European agri-food research.

Suggestions on the sharing of infrastructures at a European level:

- Improvement of the visibility of existing Research Infrastructures for example, by establishing a common database on existing infrastructures for agri-food research
- Optimisation of researchers' mobility and fostering of joint meetings, regular exchanges of visits and discussions
- Creation of trans-national (or even European) research programmes
- Standardisation and harmonisation of protocols, methodologies, equipment and data acquisition
- Strengthening of governance with, for example, a European board set up for coordination between the countries and the institutes, and with the elimination of administrative barriers
- Further usage and development of existing European programmes (e.g. ERA-Net, COST actions ...), and existing thematic working groups

<sup>8</sup> Report from the Collaborative Working Group "Shared Infrastructures for European agri-food research" (SCAR CWG) to the Standing Committee on Agricultural Research (SCAR)

- Establishment of better communication
- Strengthening of national and international cooperation
- Support of interdisciplinary research
- Sustainability of financial support of specific EU partnering programmes

The agri-food sector in Europe is facing important challenges such as the adaptation to and mitigation of climate change, food security (linked to the growing population and the change in food consumption patterns), energy security (linked to the scarcity of fossil fuel and bioenergy development), biodiversity and natural resource management (including soil and water), food safety (including animal/human health and animal welfare) and nutrition (obesity and malnutrition). It is now recognised that coordinated efforts are needed to help the scientific community to cope with these challenges and the SCAR CWG's survey is a first attempt to systematically respond to the important future challenges with respect to Research Infrastructures in the agri-food domain.

The SCAR CWG's survey will contribute to the development of strategic approaches in the agri-food domain. The objective is to identify those research domains for which shared Research Infrastructures will be crucial in the future for an effective and robust agriculture knowledge system. Of great interest is the analysis of the motivations for a shared infrastructure initiative. In that respect the SCAR CWG's survey report helps in defining how agricultural research could be embedded in the field of Biological and Medical Sciences of the ESFRI Roadmap. Moreover, it identifies some research themes of interest for agricultural and agri-food Research Infrastructures:

- Agriculture and climate change – in terms of agricultural practices and ecosystems ecology
- Agricultural systems, especially soil quality, forestry monitoring, plant genetics and physiology (i.e. photosynthesis, responses to biotic and abiotic stress seed and root development), livestock

management, animal genetics, physiology, health and welfare, plant pests and diseases, phenotyping, fisheries and aquaculture

- Biological resources as food and feed sciences, esp. genetic and biological resources, including gene banks, germplasm collections and databases
- Food production and consumer health, i.e. post-harvest handling, storage and processing methods, nutrition and consumer sciences, focussing on nutritional studies to address the link between food and human health, incl. i.e. epidemiological studies
- Renewable energy – esp. the improvement of biogas production plants and processes and the various options for biofuels derived from plants, algae or i.e. animal waste

### 3.3.2 ERA-Instruments – an ERA-Net initiative for promoting infrastructure funding in the Life Sciences<sup>9</sup>

During the past years manifold activities with respect to a European discussion on Research Infrastructures have developed, with ESFRI being probably the most prominent example. As a consequence, the relevance of RIs for the Life Sciences has become widely accepted. Life Sciences are a scientific area with very rapidly evolving requirements and challenges with respect to, for example, instrumentation and data handling and adequate Research Infrastructures are, therefore, of paramount importance for effective scientific work.

ERA-Instruments is aiming at initiating coordination and maintaining a sustainable network of ministries, charities, funding agencies and research councils active in funding of Life Sciences, and has recently published some of the project's results in two papers formulating recommendations on efficient operation and access as well as on funding schemes. Another activity, the

<sup>9</sup> Dr. Johannes Janssen  
Deutsche Forschungsgemeinschaft (DFG); Coordinator of ERA-Instruments; [www.era-instruments.eu](http://www.era-instruments.eu)

Member Organisation Forum on Research Infrastructures, has recently been implemented by the EuroHORCs (European Heads of Research Councils) and ESF (European Science Foundation), in order to generalise such experiences and to extend them to all kind of RIs.

The focus of ERA-Instruments is on mid-size instrumentation in the Life Sciences such as nuclear magnetic resonance, mass spectrometry, microscopy, high-throughput sequencers etc. But discussions about instrumentation and large equipment in that field will often be naturally interwoven with more general issues that relate to the Research Infrastructures that contain or operate the equipment. There is a clear tendency in Life Sciences to make shared use of instrumentation and to run it in centres like core facilities. The distributed Research Infrastructures (especially the corresponding ESFRI BMS initiatives) typically consist of such core facilities that in many cases evolved from local centres rather than being founded as major RIs from the outset.

If one investigates the resulting requirements and boundary conditions for the facilities harbouring mid-size instrumentation, as they are developing currently in many places, it appears that they show a lot of similarities with respect to best practices and requirements as they are discussed in the frame of ESFRI. For instance, if a facility offers access to its resources, issues like scientific quality, management structure, access procedures, user assistance, training, financial models for operational costs, intellectual property right - just to name a few - occur irrespective of the size or kind of the facility. Obviously, there are also differences between the various types of RIs. For instance the financial models will vary depending on the purpose of a facility. If it is directly founded as a European or national RI it will very likely be able to provide open access covering expenses from institutional funding. Facilities that emerge from existing successful scientific units may often be interested to open their resources to external users but might need financial support, e.g. in terms of user fees. Additionally, the establishment of a

professional management structure is often a challenge in these cases.

ERA-Instruments appreciates for that reason the work done in the various initiatives that focus on the elucidation of best practices and standards. Decision makers that distribute funds for investments and running costs of the existing and new facilities have to be informed how scientific infrastructures can be supported efficiently to promote research in the best possible way.

A very important outcome of recent discussions is that a lot of issues related to RIs appear rather independent of the size of a facility - may it be of European, national or even regional level. Sharing experiences and views will increase the efficiency of national and European actors in supporting science. The focus in discussions and activities should always be on quality, independent of size.

ESFRI and other stakeholders contributed to these insights so far and are encouraged to continue to do so in order to obtain a comprehensive picture of modern Research Infrastructures in Europe.

### 3.3.3 ESF's /EMRC's Strategy for medical Research Infrastructures in Europe<sup>10</sup>

The annual return on investments in medical research is more than 30% per year perpetually. The USA spends more than twice as much on medical research as Europe. Therefore we need to strengthen and improve European medical research, as this will result in better European economy, health and human welfare. In Europe and in the rest of the world we are facing rapid changes in society with globalisation, new diseases, climate changes and in Europe a changed demography with an ageing population suffering from the metabolic syndrome with obesity, diabetes, cardiovascular diseases and bone & joint problems. Medical research is essential to cope with these future challenges. To secure the European economy in the future

<sup>10</sup> Prof. Liselotte Højgaard, MD DMSc  
Chair of the Standing Committee of the European Medical Research Councils (EMRC), European Science Foundation (ESF)

we need medical research to facilitate a successful European medical industry.

Collaboration is the key word for medical research in Europe in the future, with a strong focus on basic research, clinical and translational research, bringing basic knowledge into clinical practice and vice versa. Clinical research and especially investigator-driven clinical trials are under strain in Europe for a multiplicity of reasons and should be particularly strengthened. Medical research should be facilitated by interdisciplinary approaches and through private public partnership. Education and career track schemes that provide attractive opportunities for researchers are essential.

Europe must invest in national and European medical RIs as indicated in the ESFRI Roadmap. Excellent world class RIs are needed in the field of medical research with emphasis on collaboration. In a recent comparison between medical research in the USA and Europe the medical research area is not only underfunded in Europe compared to the USA but also fragmented and with a low level of collaboration.

The Grand Challenges of tomorrow in Europe will need the establishment of large European medical RIs, as we can only meet the needs and deliver the future solutions if we work together and have state of the art RIs such as those on the ESFRI Roadmap.

Medical research is performed by research groups in hospitals and by large collaborative groups in major Research Infrastructures. Personalised medicine is already here in the everyday clinical patient treatment in the hospitals in Europe. We need the large ESFRI infrastructures to develop the future concept of medicine into a true personalised, predictive and pre-emptive model.

Partnership is needed in Europe among institutions and investments in infrastructures should be planned so that the new EU Member States can release their large intellectual potential. This will create an optimal environment for medical research across the whole of Europe.

### 3.3.4 European Commission<sup>11</sup>

With the widespread use of molecular biology in almost every research laboratory, and with the refinement of imaging tools at all scales, RIs have become essential tools for researchers in the Life Sciences, especially during the past 20 years.

Historically, RIs have largely been funded at a national level. While some countries make significant investments in RIs and some Member States have supported the establishment of inter-governmental organisations such as CERN, EMBL, European Synchrotron Radiation Facility (ESRF), etc. that operate RIs it is now becoming very difficult for one single country to provide all of the required state of the art facilities. In addition, in the less research intensive countries, the high investment and operation costs and/or smaller local demand have been a barrier to national investment in required RIs.

A concerted European Union approach is needed that will reduce fragmentation of national efforts, allow critical mass with higher visibility, help financial engineering between countries, avoid unnecessary overlaps while generating economies of scale, help Europe to attract the best scientists, and also standardise protocols and data management across the continent.

Over the successive research Framework Programmes of the European Union it has been recognised that the European scientific community needs RIs to remain at the forefront of excellent research and to generate a knowledge triangle attractive to industry. The current FP7 Capacities Programme for RIs aims to develop existing RIs in Europe to ensure optimal use and to facilitate the creation of new RI in all fields of science and technology.

Starting in FP2 (with around 30 Million ECU), the EU Framework Programmes have gradually increased their allocation to RIs. The current FP7 allocation now stands at € 1.7 billion.

FP7 gives support to existing infrastructures though the so-called "Integrating Activities"

<sup>11</sup> Jean-Emmanuel Faure; European Commission, DG Research

(~ € 630 Million). Each Integrating Activity project supports financially the access of researchers to key facilities and resources located outside their own country, the networking of key infrastructures, as well as joint research projects to improve their performance. Integrating Activity projects thus help the way RIs operate and promote their coherent use and development throughout Europe.

In addition FP7 supports information and communications technology (ICT) based e-infrastructures (~ € 420 Million), in particular for the development and evolution of high-capacity/high-performance communication, grid, and high performance computing infrastructures.

Through "Design studies" (~ € 50 Million), FP7 supports feasibility studies to promote the emergence of new RIs. FP7 also supports the "Preparatory Phase" of all ESFRI initiatives (~ € 190 Million), aiming at solving all issues (legal, governance, financial or technical) that are critical for the realisation of the infrastructures. An additional support to constructions comes from FP7 either through direct support (~ € 130 Million), or through the Risk Sharing Finance Facility, RSFF (~ € 200 Million).

As of today, 60 Integrating Activities and 45 Preparatory Phase projects, in all fields of science and technology, have been selected for funding under FP7. In the domain of Life Sciences, 16 Integrating Activities and 10 Preparatory Phase projects, plus a few additional projects, with a total EU contribution of more than € 180 Million, are

already funded or under negotiations. All these projects now cover the broad range of Life Sciences, from bioinformatics resources, biological resource centres, -omics facilities, to imaging facilities, animal bio-safety laboratories, or aquaculture research facilities, etc.. Figure 3 summarises the current FP7 support to Life Sciences RIs, and gives an overview on how these FP7 projects correspond to national priorities, ESFRI initiatives, Grand Challenges, Joint Programming Initiatives and other policies, with the view of strengthening research and innovation in Europe, at the horizon 2020.

Another major support from the European Union comes from the Regional Policy, with the allocation of Structural Funds to RIs projects. Indeed, € 10 Billion are earmarked under the current Financial Perspectives for "R&TD infrastructure and centres of competence", which could boost the competitiveness of European Research Infrastructures. Both national RIs and RIs listed on the ESFRI Roadmap could benefit from these funds.

Besides financial support, an important effort of the European Union over the last few years consisted in developing a new legal framework tailored to the setting up of new European RIs. It is expected that the new Community legal framework ERIC, proposed by the Commission and adopted by Council in June 2009 as a regulation, will facilitate the collaboration between European countries for the setting up and operation of new RIs (several applications are now under preparation).

	National Roadmaps														ESFRI	FP7 Research Infrastructure projects	Grand Challenges - Linked initiatives and policies											
	CZ	EE	EL	ES	FI	FR	IE	IT	NL	NO	RO	SE	UK	GC Climate			GC Energy	GC Environment	GC Health-Ageing	GC Transport	JPI Ageing	JPI Agri-Food	JPI Diet	JPI Micro	JPI Neuro	IMI	Other policies	
Bioinformatics resources	Life Science data resources																											
	Systems biology resources																											
	Chemical libraries, screening platforms, drug development facilities																											
	Microbial resources																											
	Virus archives																											
Biological Resource Centres	Mosquito repositories																											
	Mouse repositories and phenotyping centers																											
	Non-human primate centers																											
	Biobanks and biomolecular resources																											
	Cohorts																											
Omics facilities	Native seed banks																											
	Marine biology resources																											
	Animal genetic resources																											
	Plant genetic resources																											
	High throughput genomics facilities (sequencing, genotyping, etc.)																											
Imaging facilities	Transcriptomics facilities																											
	High throughput proteomics facilities																											
	Structural biology facilities (NMR, X-ray crystallography, protein production, etc.)																											
	High throughput metabolomics facilities																											
	Imaging facilities: electron microscopy, light microscopy, medical imaging, etc.																											
Medical research facilities	BSL4 laboratories																											
	Translational research facilities																											
	Clinical research facilities																											
	Vaccine development platforms																											
	GMP facilities for gene/cell therapies																											
Food and agriculture research facilities	Hadron therapy facilities																											
	Research oriented surgery/operating theaters																											
	Animal BSL2 and BSL3 facilities																											
	Aquaculture research facilities																											
	Animal farms, livestock management facilities																											
	Food analysis and processing facilities																											
	Plant phenotyping facilities																											
	Research facilities for biomass conversion and biorefinery																											

Figure 3: Major classes of Research Infrastructures for the Life Sciences

### Figure 3 - legend:

#### Roadmaps

**CZ:** Czech Republic Roadmap, 2010  
([www.msmt.cz/vyzkum/schvaleny-text-cestovni-mapy](http://www.msmt.cz/vyzkum/schvaleny-text-cestovni-mapy))

**EE:** Estonia Roadmap, 2010  
([www.etis.ee/portaal/includes/dokumendid/teekaart.pdf](http://www.etis.ee/portaal/includes/dokumendid/teekaart.pdf))

**EL:** Greek Roadmap, 2007  
([www.gsrt.gr/default.asp?FILE=items/5899/149](http://www.gsrt.gr/default.asp?FILE=items/5899/149))

**ES:** Spanish Roadmap, 2010  
([www.micinn.es/stfls/MICINN/Investigacion/FICHEROS/Building%20the%20science%20of%20the%2021st%20century%20con%20portada.pdf](http://www.micinn.es/stfls/MICINN/Investigacion/FICHEROS/Building%20the%20science%20of%20the%2021st%20century%20con%20portada.pdf)),  
and document 2007  
([ftp://ftp.cordis.europa.eu/pub/esfri/docs/spa\\_nish-singular-scientific-infrastructures\\_en.pdf](http://ftp.cordis.europa.eu/pub/esfri/docs/spa_nish-singular-scientific-infrastructures_en.pdf))

**FI:** Finnish Roadmap, 2009  
([www.tsv.fi/tik/kansallisen\\_tason\\_tutkimusinfrastruktuurit\\_tiivistelma\\_englanti.pdf](http://www.tsv.fi/tik/kansallisen_tason_tutkimusinfrastruktuurit_tiivistelma_englanti.pdf))

**FR:** French Roadmap, 2008  
([www.roadmaptgi.fr/Documents/roadmap\\_complete\\_2\\_decembre\\_mcgs\\_mc.pdf](http://www.roadmaptgi.fr/Documents/roadmap_complete_2_decembre_mcgs_mc.pdf))

**IE:** Irish Roadmap, 2007  
([ftp://ftp.cordis.europa.eu/pub/esfri/docs/ireland-and-roadmap.pdf](http://ftp.cordis.europa.eu/pub/esfri/docs/ireland-and-roadmap.pdf))

**IT:** Italian Roadmap, 2010

**NL:** Dutch Roadmap, 2008  
([www.minocw.nl/documenten/Dutch%20Roadmap%20Eng.pdf](http://www.minocw.nl/documenten/Dutch%20Roadmap%20Eng.pdf))

**NO:** Norwegian Roadmap, 2008  
([www.roadmaptgi.fr/Documents/Norwegian%20strategy.pdf](http://www.roadmaptgi.fr/Documents/Norwegian%20strategy.pdf))

**RO:** Romanian Roadmap, 2007  
([www.mct.ro/img/files\\_up/1242293614cric\\_eng.pdf](http://www.mct.ro/img/files_up/1242293614cric_eng.pdf))

**SE:** Swedish Roadmap, 2007  
([www.vr.se/download/18.76ac7139118ccc2078b800011963/Rapport+5.2008.pdf](http://www.vr.se/download/18.76ac7139118ccc2078b800011963/Rapport+5.2008.pdf))

**UK:** United Kingdom Roadmap, 2008  
([www.rcuk.ac.uk/cmsweb/downloads/rcuk/publications/lfrroadmap08.pdf](http://www.rcuk.ac.uk/cmsweb/downloads/rcuk/publications/lfrroadmap08.pdf))

**ESFRI:** European Strategy Forum for Research Infrastructures Roadmap, 2008  
(<http://cordis.europa.eu/esfri/>)

#### Grand Challenges - Linked initiatives and policies

**GC Climate:** Grand Challenge "Climate change and resource efficiency" of the European Strategy "EU2020"  
([http://ec.europa.eu/eu2020/index\\_en.htm](http://ec.europa.eu/eu2020/index_en.htm))

**GC Energy:** Grand Challenge "Energy and resource efficiency" of the European Strategy "EU2020"  
([http://ec.europa.eu/eu2020/index\\_en.htm](http://ec.europa.eu/eu2020/index_en.htm))

**GC Environment:** Grand Challenge "Environmentally-friendly production methods and land management" of the European Strategy "EU2020"  
([http://ec.europa.eu/eu2020/index\\_en.htm](http://ec.europa.eu/eu2020/index_en.htm))

**GC Health-Ageing:** Grand Challenge "Health and Ageing" of the European Strategy "EU2020"  
([http://ec.europa.eu/eu2020/index\\_en.htm](http://ec.europa.eu/eu2020/index_en.htm))

**GC Transport:** Grand Challenge "Transport" of the European Strategy "EU2020"  
([http://ec.europa.eu/eu2020/index\\_en.htm](http://ec.europa.eu/eu2020/index_en.htm))

**IMI:** Innovative Medicine Initiative ([www.imi-europe.org](http://www.imi-europe.org))

**JPI Ageing:** Joint Programming Initiative proposal on "More Years, Better Lives"  
([www.era.gv.at/attach/JPIMoreYears-BetterLives2010-05-04.pdf](http://www.era.gv.at/attach/JPIMoreYears-BetterLives2010-05-04.pdf))

**JPI Agri-Food:** Joint Programming Initiative proposal on "Agriculture, food security and climate change"

**JPI Diet:** Joint Programming Initiative proposal on "Health, food and prevention of diet-related diseases"

**JPI Micro:** Joint Programming Initiative proposal on "Antimicrobial resistance"  
([www.era.gv.at/attach/JPIAntimicrobialResistance2010-05-04.pdf](http://www.era.gv.at/attach/JPIAntimicrobialResistance2010-05-04.pdf))

**JPI Neuro:** Joint Programming Initiative on "Neurodegenerative diseases, in particular Alzheimer's disease"

**SCAR:** Report from the Standing Committee on Agricultural Research Collaborative Working Group on Infrastructures, 2009



## 4 PROGRESS OF BMS RIs

### 4.1 Introduction

The mandate of the BMS TWG comprises the monitoring of the progress of each of the RIs already on the Roadmap. The last update of the ESFRI Roadmap, published in 2008 included altogether 10 mature Research Infrastructures from the Biological and Medical Sciences sector (6 RIs from the first generation, ESFRI Roadmap 2006, and 4 RIs of the second Roadmap 2008).


For this report all 10 BMS RIs have updated their self-descriptions to allow the BMS TWG to advise ESFRI on the progress and whether projects should remain on the next edition of the Roadmap.

To give the most important information at first glance each synopsis starts with a figure, including a map indicating the Preparatory Phase partners via a 2-colour-code (dark blue for Member States with partners and light blue for Member States with associated partners, if applicable). Furthermore, information on PP costs, construction costs, operation costs, number of partners, and the internet address is given.

The coordinators of the RIs focused on the main characteristics especially with regard to the scientific and concept case of the respective Research Infrastructure. These documents, based on the templates that were filled in to apply for inclusion in the ESFRI Roadmap, also include further information on the strategic importance of the RIs in providing the ERIL to provide the essential underpinning foundations for the ERA.

More generally, a full range of other socio-economic impacts are identified. Lists of participating members, information on budgetary conditions and timetables are given. The 6 first generation BMS RIs give an account of the progress in their European Commission funded Preparatory Phases.

A table reflecting the networking of RIs in the BMS area is included at the end of each of the 10 BMS RIs self-descriptions. The legend for these tables is as follows:

<b>Thematic link (with further specification)</b>	
<b>Technological link (with further specification)</b>	
1 <sup>st</sup> generation RI	
2 <sup>nd</sup> generation RI	
Other ESFRI Groups	
Direction of link: (uni-/bidirectional)	

At its meetings and at regular intervals the BMS TWG received presentations by the individual RIs about their progress. BMS TWG held in depth discussions on bottlenecks and shared advice on how to overcome them. The BMS TWG monitored at each TWG meeting the commitment of the Member States to the various RIs. All of that put the BMS TWG into the position to advise ESFRI that all BMS RIs should remain on the Roadmap.

### 4.2 The 6 first generation BMS RIs

After having successfully applied for the FP7 call for proposals in the Specific Programme Capacities (see "Call FP7-INFRASTRUCTURES-2007-1"), all 6 BMS RIs of the first generation signed their respective contracts for their Preparatory Phases with the European Commission in 2007. The main objective of the PPs is to provide catalytic and leveraging support, helping RIs to reach the level of technical, legal, and financial maturity required to enable their construction. The PPs started between the end of 2007 and the beginning of 2008 respectively. As for most of the RIs the Preparatory Phase duration was expected to be three years, the PPs will be completed at the end of 2010/early 2011. The EC contribution to the consortia is between 4.2 and 5.8 Mio €. The number of partners within these RI initiatives varies between 17 and 53.

Subsequent to the PPs, the BMS RIs will tackle the next steps towards implementation – the start of the construction phase. The estimated costs for construction range from 20 Mio € (depending on the number of hubs/nodes) to

470 Mio € in total. Between 3 Mio € up to 100 Mio € have to be calculated per year for operation depending on the RI.

#### **4.3 The 4 second generation RIs**

Four BMS proposals were identified as promising RI initiatives when the last update of the BMS Report occurred in 2008. They all fully met the ESFRI criteria for inclusion in the ESFRI Roadmap 2008.

In 2009 the European Commission published a call for proposals in the Specific Programme Capacities (see "Call FP7-INFRASTRUCTURES-2010-1; call N°6"). 4 (out of 11 topics) were targeted at initiatives from the Life Sciences sector. The aim of this call was to give support to RIs identified in the 2008 ESFRI Roadmap to reach the level of technical, legal and financial maturity required to enable the construction work to start. Thereby, as with the 6 first generation RIs, the Preparatory Phase will contribute to the technological development capacity and to the scientific performance and attractiveness of the European

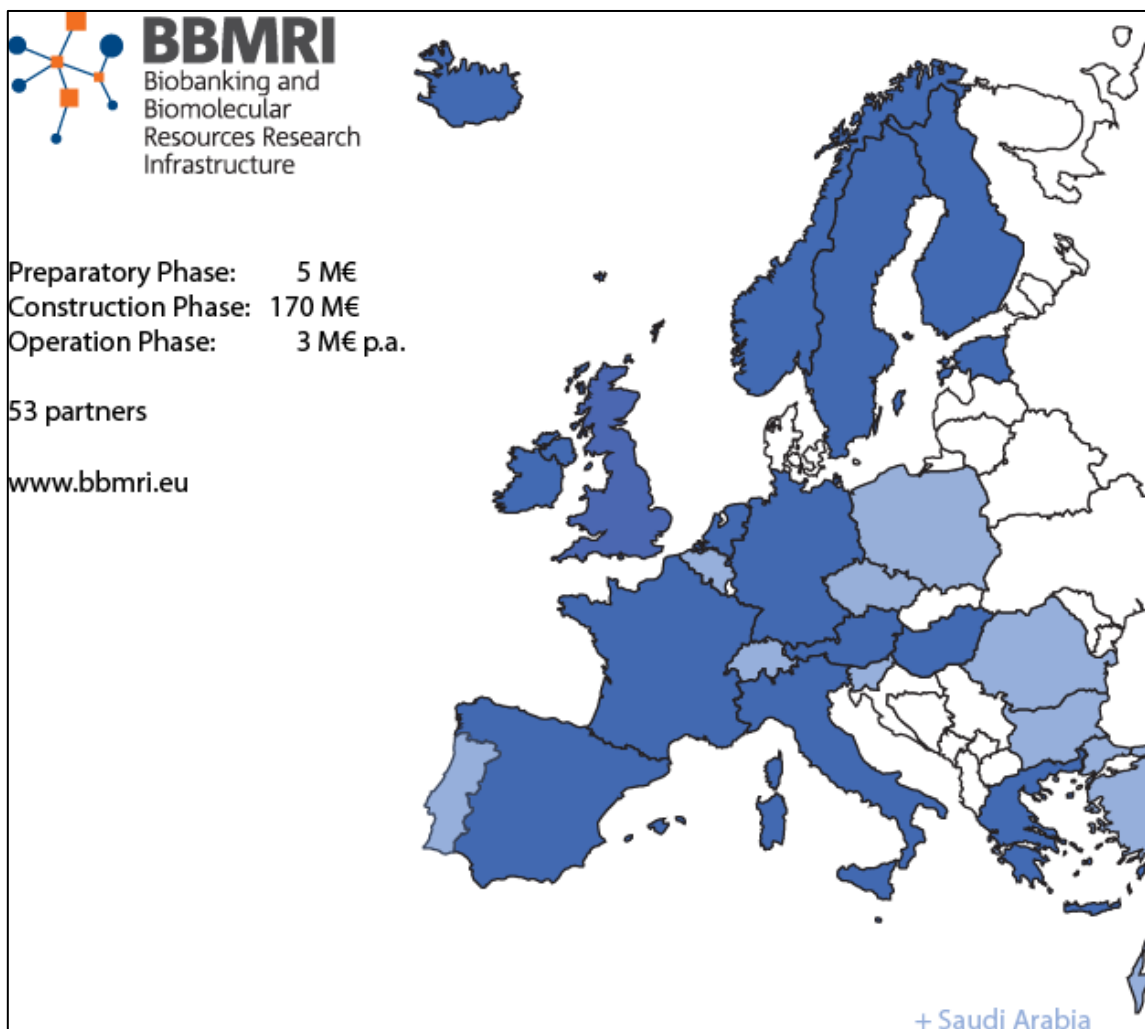
Research Area. The call closed at the end of November 2009 and all 4 BMS proposals were evaluated with very high scores. Accordingly, the consortia negotiated their initiatives in summer 2010 and will start their PP at the end of 2010.

#### **4.4 Promoting synergies**

To strengthen the BMS RIs implementation phases the European Commission recently published an additional call for proposals in the Specific Programme Capacities (see "Call FP7-INFRASTRUCTURES-2011-1; call N°8"). The main objective of the activity "Implementation of common solutions for a cluster of ESFRI Infrastructures in the field of Life Sciences" is to support them to advance in their construction, promoting synergies among initiatives in the same field. In addition they will strengthen the implementation of common solutions to respond to common needs, thereby fostering harmonisation, cost-efficiency and interoperability.

## 4.5 Descriptions of the 6 first generation BMS RIs

### 4.5.1 Biobanking and Biomolecular Resources Research Infrastructure (BBMRI)



The Preparatory Phase of BBMRI is funded by the European Commission with 5.0 Mio €. Started in February 2008, the consortium today consists of 53 partners (including 19 ministries and funding organizations) and 220 associated organizations from 33 countries as shown on the map above.

Human biological samples, such as blood, tissues, cells or DNA that are associated with clinical and research data are considered as essential raw material for the advancement of biotechnology, human health and research and development in Life

Sciences. BBMRI will build on existing sample collections, resources, technologies, and expertise, which will be specifically complemented with innovative components. In particular, BBMRI will comprise i) all major population-based and disease-oriented biobank formats, ii) biomolecular resources, such as collections of antibodies and other affinity binders and a variety of molecular tools to decipher protein interactions and function, iii) bio-computing and sample storage infrastructure (see Figure 4), iv) scientific, technical as well as ethical and legal expertise.



**Figure 4:** Hermetic semi-automated cryostorage system

All resources will be integrated into a pan-European distributed network structure, and will be properly embedded into European scientific, ethical, legal and societal frameworks. Specific tasks in the planning of

BBMRI include the generation of an inventory of existing resources, technologies and know-how that serve as building blocks of BBMRI, the implementation of common standards and access rules, the establishment of incentives for resource providers, and the development of solutions that facilitate international exchange of biological samples and data which properly consider the heterogeneity of pertinent national legislation and ethical principles. For the construction phase BBMRI plans to adopt the European Research Infrastructure Consortium (ERIC) legal framework that supports the distributed architecture of BBMRI with operational sites in multiple Member States. Austria has offered to host the headquarters of BBMRI-ERIC and several Member States have officially expressed their interest in becoming members of BBMRI-ERIC and in committing funding for its operation. Construction and start of operation is foreseen for the end of 2011.

### **1. Name and descriptive title**

## **BBMRI - Biobanking and Biomolecular Resources Research Infrastructure**

### **2. Short description of new RI or major upgrade and main characteristics**

Human biological samples, such as blood, tissues, cells or DNA, plus associated clinical and research data, as well as biomolecular research tools are key resources in unravelling genetic and environmental factors underlying diseases and influencing their outcome. Furthermore, these resources are required for identification of new targets for therapy and may help to reduce attrition in drug discovery and development. Consequently, biological resources are considered as the essential raw material for the advancement of biotechnology, human health and research and development in Life Sciences. The pan-European Biobanking and Biomolecular Resources Research Infrastructure (BBMRI) is designed to further develop these resources and to provide access to academia and industry.

BBMRI builds on existing sample collections, resources, technologies, and expertise, which will be specifically complemented with innovative components. In particular, BBMRI comprises i) all major population-based and disease-oriented biobanks, ii) biomolecular resources, such as collections of antibodies and other affinity binders and a variety of molecular tools to decipher protein interactions and function, iii) bio-computing and sample storage infrastructure, iv) scientific, technical as well as ethical and legal expertise. All resources will be integrated into a pan-European distributed hub structure-like network, and will be properly embedded into European scientific, ethical, legal and societal frameworks. Specific tasks in the planning of BBMRI are the preparation of an inventory of existing resources, achieving interoperability by implementation of common standards and access rules, establishment of incentives for resource providers, and to develop solutions for international exchange of biological samples and data which properly consider the heterogeneity of pertinent national legislation and ethical principles.

BBMRI will become an interface between patients as well as populations of European countries and top-level biological and medical research and at the same time operates as a firewall by preventing inappropriate flow of information between donors and researchers. This can only be achieved by a distributed Research Infrastructure with operational units in most if not all European Member States. It is planned to implement BBMRI under the ERIC (European Research Infrastructure Consortium) legal entity. BBMRI-ERIC foresees a headquarters in one Member State that coordinates the interaction of national hubs established in several Member States. The headquarters will provide a common access portal to resources available in Member States as well as appropriate facilities and expertise. The national hubs are also established under the ERIC legal entity and will link the national scientific community (e.g., universities, hospitals, research institutions, resource centres) to BBMRI-ERIC.

### **3. Scientific Case**

Following the rapid progress in genomics research of humans and their ancestors, biomedical and health research has expanded from the study of rare monogenic diseases to common, multifactorial diseases. Innovative, high-throughput technologies are widely expected to enable a better dissection of these complex, causally heterogeneous diseases into more specific diagnostic entities, which is a requirement for the advancement of personalised medicine. A sharper, biology-based definition of disease categories will enhance the development of more effective treatment, reduce undesired side effects of new treatments, improve success in clinical trial design, and will lead to new concepts of disease prevention. Elucidation of complex disease aetiology is challenging because diseases are caused by a large number of small, often additive effects, representing the sum of the consequences of genetic predisposition, lifestyle and the environment.

Revealing these complex interactions will depend critically on the study of large sets of well-documented, up-to-date epidemiological, clinical, biological and molecular information and corresponding material from large numbers of patients and healthy persons, collected and made available by biobanks. The biological material collected in biobanks for biomedical research typically comprises DNA, tissues, cells, blood, other body fluids as well as pathogen-containing biological samples. Although currently established biobanks and biomolecular resources are a specific European strength, valuable and irreplaceable national collections typically suffer from fragmentation of the European biobanking-related research community, variable access rules, the lack of commonly applied standards, lack of interoperability of clinical, analytical and -omics datasets required for research and a diversity of legal procedures and ethical considerations. This hampers the collation of biological samples and data from different biobanks which is a prerequisite to achieving sufficient statistical power and to avoid selection bias. Moreover, it results in duplication of effort and jeopardises sustainability because of the lack of long-term comprehensive funding approaches.

There is also a need to strengthen the capacity to develop networks of biobanks meeting high standards of integration compatible with the design of studies structured as phase II or III clinical trials. This type of study design is essential for validation and translation of biomarkers into clinical practice.

Ultimately, BBMRI will favour the study of important biomedical research questions that are beyond the scope of efforts of single Member States. Short-term benefits will appear soon, such as increased quality and reduced cost of research through better coordination, while longer perspectives include increased efficacy of drug discovery and development, and finally novel possibilities in health care (such as personalised medicine) and secured European competitiveness in research and health-related economy.

#### **4. Concept Case**

The Preparatory Phase of BBMRI started on 1<sup>st</sup> February, 2008. By January 2010, the consortium consisted of 53 participants (including 19 funding organizations) and more than 200 associated organizations from 33 European and third countries.

Key components of BBMRI are collections of biological samples from different (sub-) populations and patients of Europe, which should in a secure manner be linked and continuously updated with data on the health status, lifestyle and environmental exposure of the sample donors. This can only be achieved in a federated network of centres established in most, if not all, European Member States. The IT infrastructure which employs federated database architecture will integrate the complex network of hubs, members and partners to facilitate interoperability, to provide one common access point, and to guarantee privacy. Consensus was found on a general information management system for maintaining unique and secure coding systems for specimens, subjects and biobanks. The users may come from different fields of academia and industry. Access will be provided in the context of specific top-quality research projects approved by independent expert boards as well as research ethics committees. Incentives are foreseen for EU Member States to become member of BBMRI and for industry to enter into (non-for-profit or pre-competitive) public-private partnerships or general user agreements.

BBMRI will use available resources, technologies and expertise as building blocks. Therefore a comprehensive inventory of existing population-based and clinical or disease-orientated biobanks in Europe has been established. A core questionnaire was supplemented with a total of ten supplementary questionnaires dealing with detailed information on issues such as available resources, standardisation of procedures, data collection and handling, IT solutions as well as legal and ethical issues and funding. The data collected are stored in an interactive catalogue supporting "on-demand" queries against participating biobanks thereby serving as prototype of a search tool to allow users to define studies requiring access to BBMRI. The catalogue currently includes metadata and aggregate data from 247 Biobanks and 21 countries

providing overview on a total of more than 16 million samples.

Furthermore, existing biomolecular resources and molecular tools applicable to biobanking have been reviewed. This has led to a new community standard of affinity reagents (MIAPAR), designed to tackle the problems of scattered information and imprecise descriptions and to facilitate database implementation. In addition, a new database for molecular methods has been established, providing best practice-based protocols for molecular analyses of different types of samples.

The concept on ethics related policies for biobanks and biomolecular resources is based on analyses on the ethical, social and legal issues related to the infrastructure. A WIKI+ platform for legal aspects of biobanks is provided as supportive tool. An online platform on legal aspects for uploading and validating existing legal documents in use in BBMRI Member and Partner countries is under development and a tool (hSERN=human sample exchange regulation navigator) previously conceived for facilitating the access to regulation on sample exchange throughout Europe has been improved and open on the web.

A data protection group provides guidance on the cross-border data transfer related to BBMRI. Building on existing knowledge on both legal and IT aspects, the data protection group will identify cross-border data protection issues associated with the deliverables of BBMRI, and explore the potential of Privacy Enhancing Technologies (PETs), which allow for IT solutions to legal issues and challenges. Any such approaches will be tested against and based on the common minimum standards set by the European Union for "the protection of individuals with regard to the processing of personal data and on the free movement of such data".

To provide efficient access to industry the establishment of BBMRI expert centres is foreseen, which is a new model of a pre-competitive, non-profit private-public-partnership that integrates public biological resources as well as expertise and equipment from academia and industry. This should result in increased competitiveness, and generate more value for society in agreement with requirements of the ERIC legal entity (see below).

Analysis of the cost and funding streams of biobanks have revealed that Member States have massively invested in the construction and running of their biobanks during the past decades. For biobanks associated to BBMRI the annual funding is estimated to be about 150 Mio €, this excludes funding of research projects. About 50% of the annual budget is an investment in required scientific and technical personnel. In comparison, the annual cost of integration of these biobanks in one pan-European infrastructure is about 10% of the total cost.

For sustainable operation of BBMRI close interaction with the European public(s) is essential. BBMRI has launched a comprehensive consultation and engagement process with its broad stakeholder community, comprising patients, clinicians, funding organizations, associated project partners, industry, users, but also the general public. The BBMRI stakeholders' forum plays a key role in stimulating discussion and keeping the European public(s) informed about the intentions and the progress of BBMRI.

The ERIC legal entity has been identified as the most appropriate legal entity to support the distributed operation of BBMRI. A headquarters that will provide a common access portal as well as several national hubs located in different Member States should be established within BBMRI-ERIC. Several Member States have ranked BBMRI with high priority in their national roadmaps and committed funding for national participation in BBMRI-ERIC (e.g., NL 22.5 Mio €, IT 15 Mio €, AT 14 Mio €, DE 14 Mio €, SE 14 Mio €, NO 10 Mio €, EL 5 Mio €, CZ 4.8 Mio €, FI 2.5 Mio €). Furthermore, ES, EE, BG, MT, LV, HR have officially expressed their interest to become member of BBMRI-ERIC.

**Steps towards construction of BBMRI-ERIC:**

- |   |         |
|---|---------|
| • Offer from Austria to host the BBMRI headquarters | 4Q 2009 |
| • Agreement on headquarters                         | 1Q 2010 |
| • BBMRI-ERIC statutes and business plan             | 3Q 2010 |
| • Submission of application to obtain ERIC status   | 4Q 2010 |
| • Establishment of BBMRI-ERIC                       | 3Q 2011 |
| • Start of operation with charter members           | 4Q 2011 |
| • Expansion   | >2012   |

**5. Further information, including strategic importance to ERA**

BBMRI provides the key biological resource to address several of the upcoming grand challenges for Europe, particularly in the health area and lays by its distributed architecture established under the ERIC legal framework the foundation towards improved circulation of researchers, knowledge and technology as defined in the 2020 Vision for the EU.

Over the last two decades, Europe has lost some ground in scientific issues, especially in the Life Sciences. The global networking component of BBMRI will ensure that what will be developed in Europe will have an important global impact. Europe will serve as a model for other regions and thereby enhance its scientific credentials. To balance the need, on one hand, for Europe to retain leadership in science and, on the other, to provide global solutions, thus sustaining the development and the use of biological resources, is one major aim of BBMRI. This will be achieved in that BBMRI builds on the OECD best practice guidelines for biological resource centres which define common standards for international collaborations of biological resource centres within OECD Member States. In a pilot project BBMRI tests the feasibility of how to interact with resource centres in OECD Member States and enhanced engagement countries. By this process BBMRI should also become the European component of the OECD Global Biological Resource Centres Network (GBRCN).

BBMRI involves in its Preparatory Phase currently more than 270 institutions from more than 30 countries which underlines the pan-European scope. Nevertheless there is a marked dominance of western European Member States. In the context of European Cohesion Policy BBMRI promotes participation of new Member States with its distributed architecture, by the adoption of the ERIC legal framework, specific education and training programmes and start-up packages to foster development of high quality biobanks and biological resource centres.

BBMRI is instrumental in implementing European science policy priorities such as the 2000 Lisbon Agenda, the 2020 Vision for the EU, and the Second Programme of Community Action in the Field of Health 2008-2013. By developing synergies between BBMRI and other Biological and Medical Sciences Research Infrastructures on the ESFRI Roadmap, and by the integration of the Research Infrastructures into a European BMS Research Infrastructure landscape an unprecedented momentum and opportunity are generated to strengthen Europe's competition in the Life Sciences in academia and industry.

**6. Identification of other socio-economic impacts**

The EU's ageing population is resulting in an increase in certain diseases, increased health care expenditure for people in old age that place pressure on the sustainability and viability of the EU's healthcare systems. New threats to health have emerged, such as pandemics, bioterrorism and physical and biological incidents as well as to solve the problem of climate change and new security threats. BBMRI will speed up development of medicine and disease prevention and will embrace some of the needs of basic research as well as of the biotech and pharmaceutical industries. Thus, it will provide the infrastructural basis to address emerging challenges in health care, and enables improvements in public health and will help some bottlenecks in the drug discovery and development process. BBMRI will also strongly boost



political and scientific momentum to harmonise ethical, legal and quality standards across Europe.

BBMRI is carrying an evaluation of the socio-economic impact of biobanks that support medical research. One leading company, Technopolis and two research institution, BETA (Univ. Strasbourg) and Fraunhofer are developing an evaluation strategy to assess the health and economic effects of coordinating the biobanking and biomolecular resources infrastructures for research across Europe. The overall study will consider the current state of the art on the issue and propose an assessment methodology with appropriate indicators to monitor BBMRI after its construction.

7. Participating Members

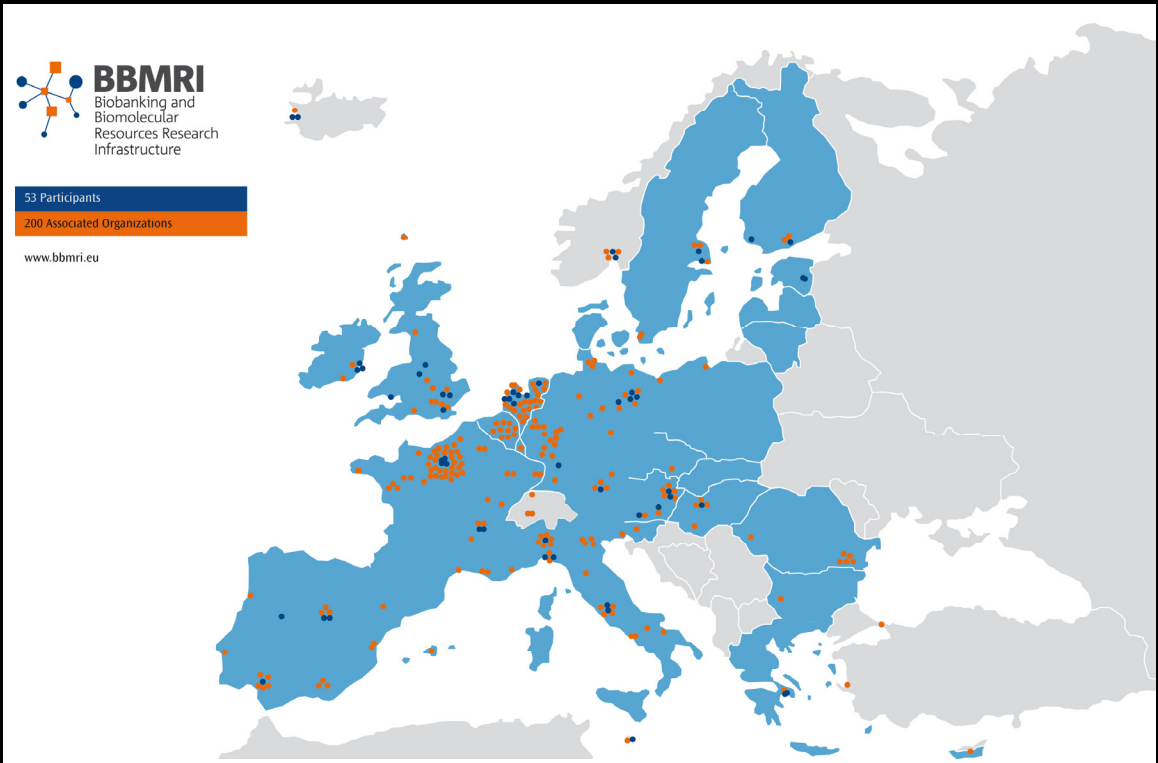


Figure 5: Overview of BBMRI Partners

This map (see Figure 5) provides an overview of BBMRI Partners and differentiates them as Participants (co-applicants of BBMRI-PP) and Associated Organisations. Associated Organisations do not have an official vote on formal issues - as Participants do have - but their input and active involvement in the project is required to ensure that the solutions developed will be suitable for future integration of the biobanks into the BBMRI structure.

<b>34 Scientific Partners</b> <ul style="list-style-type: none"><li>• Medical University of Graz, Austria</li><li>• National Institute for Health and Welfare, Finland</li><li>• National Research Center for Environment and Health, Germany</li><li>• Uppsala Universitet, Sweden</li></ul>	<b>19 Funding Organisations</b> (ministries, research councils) <ul style="list-style-type: none"><li>• INSERM, France</li><li>• Fondazione Telethon, Italy</li></ul>	<b>220 Associated Organisations</b> <table><tr><td>Australia</td><td>1</td></tr><tr><td>Austria</td><td>7</td></tr><tr><td>Belgium</td><td>10</td></tr><tr><td>Bulgaria</td><td>1</td></tr><tr><td>Canada</td><td>2</td></tr></table>	Australia	1	Austria	7	Belgium	10	Bulgaria	1	Canada	2
Australia	1											
Austria	7											
Belgium	10											
Bulgaria	1											
Canada	2											

<ul style="list-style-type: none"> <li>• Karolinska Institutet, Sweden</li> <li>• University of Manchester, United Kingdom</li> <li>• International Agency for Research on Cancer, France</li> <li>• Academisch Ziekenhuis Leiden, The Netherlands</li> <li>• Norwegian Institute of Public Health, Norway</li> <li>• University of Malta, Malta</li> <li>• Norwegian University of Science and Technology, Norway</li> <li>• Semmelweis University, Hungary</li> <li>• EGP of the University of Tartu, Estonia</li> <li>• National DNA Bank, University of Salamanca, Spain</li> <li>• Helmholtz Gemeinschaft, Germany</li> <li>• VITRO Ltd, Spain</li> <li>• Ensembl Functional Genomics, European Genotype Archive, United Kingdom</li> <li>• Erasmus MC Rotterdam, The Netherlands</li> <li>• Istituto Nazionale per la Ricerca sul Cancro, Biological Bank and Cell Factory, Italy</li> <li>• Institute for Biomedical Technologies, Italy</li> <li>• UK Biobank Ltd, United Kingdom</li> <li>• University Hospital Groningen, The Netherlands</li> <li>• Dutch Federation of University Medical Centers, The Netherlands</li> <li>• Legal Pathways b.v., The Netherlands</li> <li>• deCODE genetics, Iceland</li> <li>• Life Science Governance Institute, Austria</li> <li>• Center for Economics and Social Aspects of Genomics, United Kingdom</li> <li>• Babraham Bioscience Technologies, United Kingdom</li> <li>• Hellenic Republic Ministry of Development, General Secretariat For Research &amp; Technology, Greece</li> <li>• Biomedical Research Foundation of the Academy of Athens, Greece</li> </ul>	<ul style="list-style-type: none"> <li>• Fédération hospitalière de France – FHF, France</li> <li>• Irish Clinical Research Infrastructure Network, Ireland</li> <li>• Institut National du Cancer, France</li> <li>• Comitato Nazionale per la Biosicurezza, le Biotecnologie e le Scienze della Vita, Istituto Superiore di Sanita, Italy</li> <li>• Max-Planck-Institut für Molekulare Genetik, Germany</li> <li>• Instituto de Salud Carlos III, Spain</li> <li>• Research Infrastructure and Special Initiatives Unit Health Research Board, Ireland</li> <li>• Medical Research Council, United Kingdom</li> <li>• Ministry of Education, Culture and Science, The Netherlands</li> <li>• The Icelandic Centre for Research, Iceland</li> <li>• The Netherlands Organisation for Health Research and Development, The Netherlands</li> <li>• Fraunhofer IBMT, Germany</li> <li>• Bundesministerium für Bildung und Forschung, Germany</li> <li>• Bundesministerium für Wissenschaft und Forschung, Austria</li> <li>• Alleanza Contro il Cancro, Italy</li> </ul>	<ul style="list-style-type: none"> <li>Cyprus 1</li> <li>Czech Rep. 1</li> <li>Faroe Islands 1</li> <li>Finland 2</li> <li>France 53</li> <li>International 1</li> <li>Germany 31</li> <li>Greece 1</li> <li>Hungary 4</li> <li>Iceland 1</li> <li>Ireland 2</li> <li>Israel 4</li> <li>Italy 22</li> <li>Luxembourg 1</li> <li>Malta 1</li> <li>Martinique 1</li> <li>Norway 3</li> <li>Poland 2</li> <li>Portugal 3</li> <li>Romania 6</li> <li>Saudi Arabia 1</li> <li>Slovenia 1</li> <li>Spain 14</li> <li>Sweden 5</li> <li>Switzerland 3</li> <li>The Netherlands 23</li> <li>Turkey 2</li> <li>UK 9</li> </ul>
---	---	--

<ul style="list-style-type: none"> <li>• Universitaet Klagenfurt, Austria</li> <li>• University of Turku, Finland</li> <li>• IPPOSI, Ireland</li> <li>• Institut Mérieux, France</li> <li>• IPRI, France*</li> </ul> <p>*Subject to ongoing amendment</p>	<ul style="list-style-type: none"> <li>• Fundación para el desarrollo de la investigación en Genómica y Proteómica, Spain</li> <li>• Ministry of Education and Research, Estonia</li> </ul>	
---	---	--

### 8. Budgetary Information

Preparatory cost 5 Mio €	Construction cost approx. 170 Mio €  to be further determined in the Preparatory Phase	Operation cost for BBMRI ERIC-headquarters and Member States hubs approx. 3.5 - 5 Mio €/year.  Costs for operation of biobanks and biological resource centres in Member States (not part of BBMRI-ERIC) approx. 17 Mio €/yr.  to be further determined in the Preparatory Phase	Re- and decommissioning cost (total in Mio €)  Not applicable
-----------------------------	---	--	---

### 9. Timetable until operation

Preparatory phase  36 months	Construction phase  12 months for core infrastructure with BBMRI-ERIC founding members (start of operation 2011)	Operation  More than 30 years	Re- and decommissioning  Not applicable
------------------------------------	--	-------------------------------------	---

	36 months for fully established infrastructure		
<b>10. Contact</b>			
<p>Prof. Kurt Zatloukal, Coordinator, Institute of Pathology, Medical University of Graz, Auenbruggerplatz 25, 8036 Graz, Austria <a href="mailto:kurt.zatloukal@medunigraz.at">kurt.zatloukal@medunigraz.at</a> <a href="http://www.bbmri.eu">www.bbmri.eu</a></p> <p>Prof. Eero Vuorio, Executive Manager University of Turku Turku Centre for Biotechnology FI-20014 Turku Finland <a href="mailto:eero.vuorio@utu.fi">eero.vuorio@utu.fi</a></p>			
<b>11. Progress in the Preparatory Phase</b>			
<p><b>Key achievements</b></p> <ul style="list-style-type: none"> <li>• Available resources, technologies and expertise that serve as building blocks of BBMRI have been assessed</li> <li>• Scientific, technical, ethical and legal principles of operation and access have been defined</li> <li>• A series of tools to facilitate access have been developed</li> <li>• Proactive stakeholder involvement and public engagement</li> <li>• ERIC as legal entity has been selected</li> <li>• Offer to host BBMRI-ERIC headquarters by Austria and funding commitments from NL, SE, AT, DE, FI, NO, EL for national nodes obtained</li> <li>• Construction and start of operation 2011</li> </ul> <p><b>WP1</b> has provided the project management and has been responsible for proper integration of BBMRI into the global biobanking community as well as other science fields, particularly the other BMS Research Infrastructures. This has resulted in a joint effort of all BMS Research Infrastructures to obtain policy support from the European Parliament. Furthermore, two international conferences have been organized in collaboration with DG Research and leading biobanking organisations.</p> <p>WP1 integrates work performed by the other WPs into the operational concept of BBMRI. In collaboration with WP3 a prototype for key functionalities of BBMRI has been initiated in order to provide feasibility testing of BBMRI operational principles.</p> <p>In collaboration with WP7 the concept for BBMRI expert centres has been developed to provide efficient access to industry. Expert centres are a new model of a pre-competitive, non-profit private-public-partnership that integrates public biological resources as well as expertise and equipment from academia and industry in agreement with requirements of the ERIC legal framework.</p>			

**Stakeholder forum:** Through its activities to date, the BBMRI stakeholders' forum has created a broad, international network of stakeholders via its mechanisms for participation and feedback provision. Two major information/discussion meetings as well as a patient stakeholder workshop have been organized and a consultation document on patient participation is in preparation.

**Scientific and Ethical Advisory Board (SEAB):** SEAB members have attended all major BBMRI-PP activities. The SEAB has notably supported efforts to stimulate public-private partnerships, converging on the development of expert centres, encouraging plans for industry to consult the biobanks in a transparent and publicly accountable fashion.

**WP2** has focused on the specific requirements of population-based biobanks aiming to integrate existing European population biobank datasets into the operational concept of BBMRI. An inventory of all epidemiological collections in Europe has been performed. The collections have been identified by directly approaching all European national human genetic societies, by collecting expressions of interest and by collaborating with Public Population Project in Genomics (P<sup>3</sup>G) observatory data collection. Work towards an international network of biobanks has included the development of standard operating procedures (SOPs), analytical tools and approaches to help biobanks to collaborate in cutting-edge science for advancement of public health.

**WP3** has conducted an inventory of Europe's biobanks. Data collected via questionnaires, which in part have been developed in collaboration with P<sup>3</sup>G, are stored in an interactive catalogue ([www.bbmriportal.eu](http://www.bbmriportal.eu)). To date, the catalogue includes data from 261 biobanks and 23 countries, with a total of more than 16 million samples (submitted for publication).

Expert groups for major types of disease-oriented biobanks were established covering the topics pathology, laboratory medicine and rare diseases. A report of each expert group, including their recommendations has been released. Fourteen partners have started to collaborate in the WP3 prototype working on access rules and quality criteria. The operability of the prototype will be demonstrated by the realization of research projects on cancer and obesity/cardiovascular disease. Another task of the prototype is the extension of the BBMRI catalogue by increasing the granularity of the overview with selected prototype biobanks.

**WP4** key achievements are:

1. Defining standards and quality control for binding reagents. This has led to the standard of Minimum Information about a Protein Affinity Reagent (MIAPAR), guidelines developed in conjunction with a community of affinity reagent users to be implemented by those using and producing affinity reagents within the general research community and for their application to biobanked samples (submitted for publication).
2. Design and implementation of the Molecular Methods Database ([www.molmeth.org](http://www.molmeth.org)). MolMeth is a structured database created by WP4 partners with the aim of providing best practice-based protocols for molecular analyses of different types of samples to all BBMRI members and beyond. The database will also include protocols for sampling procedures and storage conditions.
3. A biomolecular tools and resources information portal has been constructed, including links to inventories of available binder reagent resources and molecular technologies for interrogating biobank samples at the DNA, protein and metabolite levels ([www.bbmri-wp4.eu](http://www.bbmri-wp4.eu)).

**WP5** has proposed requirements for a metadata system for European biobanks, and in consistence with these requirements demonstrated a prototype system for connecting biobank databases. Moreover, the WP has produced a first version of a multilingual lexicon with biobank-related terminology (<http://www.biobank-lexicon.org/>).

**WP6** has launched a Wiki legal platform for legal aspects of biobanks. The WIKI+ platform is available at <http://www.bbmri.eu/index.php/wiki-legal-platform>. Furthermore, WP6 has studied the concerns of various publics (e.g., lay people, patients, etc.) via a focus group and questionnaire approach. Currently, WP6 is finalising a conceptual governance model applicable to a pan-European infrastructure that includes:

- analysis of existing opinions of various Ethics committees in EU on biobanks, production of a synthetic Table and set up the bases for harmonisation regarding key areas;
- setting up a methodology and conducting pilot studies for consultation of various publics and generation of questions on biobanks for the Eurobarometer survey;
- setting up a WIKI+ platform for legal aspects of biobanks and a tool (hSERN=human sample exchange regulation navigator) for facilitating the access to regulation on sample exchange throughout Europe;
- proposal of governance models.

**WP7** was assigned the task to prepare the documents and information necessary and helpful to get the interest of countries to become founding (and funding) members of BBMRI.

A questionnaire was developed to get insight in the costs of biobanks in Europe. This information is helpful for governments and other parties to see how much is needed to set up a biobank but in certain cases also to show how much has been invested already.

A consortium of Technopolis, Beta and Fraunhofer has prepared a report evaluating the possible impact of BBMRI on science, industry and society and to provide suitable indicators for future assessment. Finally, statutes have been drafted to set up an ERIC. These have been discussed with lawyers of some countries and with the European Commission.

**Publications:**

Yuille M, van Ommen GJ, Bréchet C, Cambon-Thomsen A, Dagher G, Landegren U, Litton JE, Pasterk M, Peltonen L, Taussig M, Wichmann HE, Zatloukal K. Biobanking for Europe. *Brief Bioinform.* 2008 Jan;9(1):14-24.

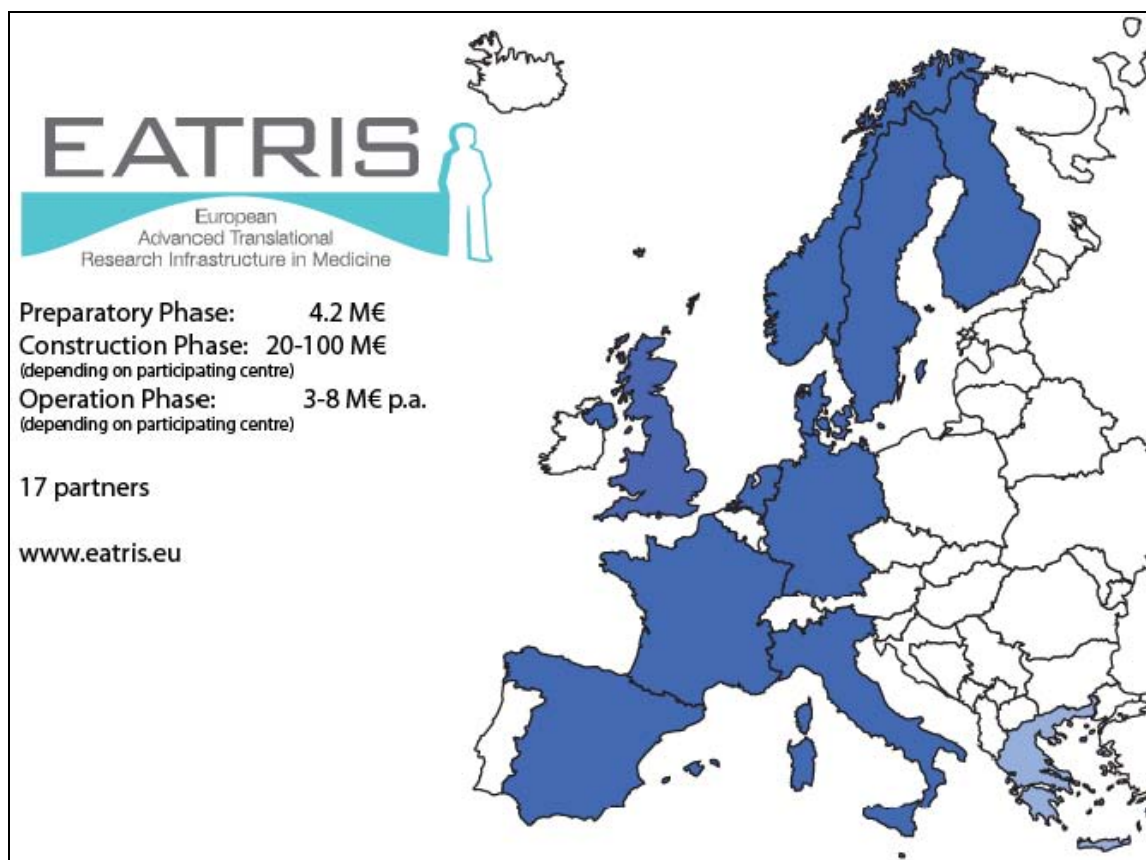
**Table 4:** Links between Research Infrastructures - BBMRI

	BBMRI	Further specification of the technological link	Further specification of the thematic link	Short statement for further specification (last update February 2010)
EATRIS	↔	Biobanking of human biological samples, access to biomolecular resources and model organisms; ethical and legal issues	Identification and verification of disease specific biomarkers, preclinical testing of new drugs and alongside clinical trial follow-up.	Access to biomaterials, patient groups, biobanking, ethical and legal issues
ECRIN	↔	Biobanking of clinical samples, ethical and legal issues	Improvement of the efficacy of clinical trials (development of companion diagnostics)	Improving the current heterogeneous European ethical and legal landscape related to medical research is a common goal
ELIXIR	↔	Common e-Infrastructure to enable the linking of biomolecular data to clinical, phenotypic and other data associated with sample collections	Enabling medical research	
Infrafrontier	↔	Banking of biological samples, disease phenotype characterization	Mapping of mouse and human phenotypic descriptions and disease ontologies	Infrafrontier's biobanking activities of mouse models of human diseases will draw on BBMRI's expertise on biobanking of human material. Mapping of disease ontologies and phenotype descriptions in man and mouse will create enormous added value
INSTRUCT	↔	Banking of proteins and gene constructs, NMR-based metabolomics	Pre-analytical standards for metabolomic studies	
EMBRC	↔	Solutions for banking of organisms and libraries, molecular tools	New model organisms for biological and biomedical research	
ERINHA	↔	Establishment of sample collection centres within health care	The establishment and management of sample collections and biorepositories associated with BSL4 laboratories; and in the harmonisation of quality, biosafety, biosecurity procedures for work with biohazardous samples including material handling and exchange within collection and repository centres	BBMRI and ERINHA will jointly establish sample collection centres for biological samples from patients infected with dangerous pathogens. This is critical to properly respond to new pandemics and to prevent bioterrorism
Euro-BioImaging	↔	Cooperative tissue image - clinical data bases	Identification of imaging biomarkers, diseases phenotype characterization based on imaging data; Correlation of new image markers with histopathological data	Euro-BioImaging will provide innovative image analysis tools for the development of biomarkers and standards for image databases.
EU-Openscreen	↔	Small molecule additions to inventory of specific ligands for human proteins (ProteinBinders)	Validated research reagents and diagnostic tools for the detection of protein targets in biological samples	
e-IRG	↔	Distributed high capacity data storage and computing		
SSH	↔	Impact of life style and social factors on health; assessment of life style and social factors, data management, privacy, biobanking	Ethical and legal issues	
ESP	↔	Innovative analytical technologies (structural biology)		
ENV	↔		Investigation of gene-environment interactions, documentation of environmental exposure	
ENE				





#### 4.5.2 European Advanced Translational Research Infrastructure in Medicine (EATRIS)



**The European Advanced Translational Research Infrastructure in Medicine, EATRIS, is a new Research Infrastructure initiative which will help Europe to fulfil its potential in the strategically critical area of translational medical research. EATRIS is a unique framework linking European countries to accelerate the development of new medicinal products by facilitating access to a new pan-European infrastructure.**

To improve human health, scientific discoveries at the level of basic biomedical research have to be “translated” into practical, clinical applications. At the same time, novel observations about the nature or progression of a disease made by clinical researchers can be passed back to inspire new approaches in basic research. This two-way process of developing new tools or treatments for use in patients is called “translational research” or “translational medicine”.

The translation of discoveries from the lab to commercially viable clinical applications is a complex and lengthy process. Basic biomedical research in Europe has traditionally been strong. However, Europe lags behind when it comes to bringing clinical innovation into clinical practice. But efficient translation of research discoveries into industrial application is an essential element to maintain Europe's competitiveness in the biomedical and health industry. The main bottleneck is the fragmented nature of science along the development chain and the limited availability of essential Research Infrastructure and know-how, leading to unacceptable delays and/or prevention of the development of new innovative medicines.

The aim of EATRIS is to fill this gap by developing a European advanced translational Research Infrastructure consisting of key preclinical and clinical facilities and translational expertise necessary to support the development of

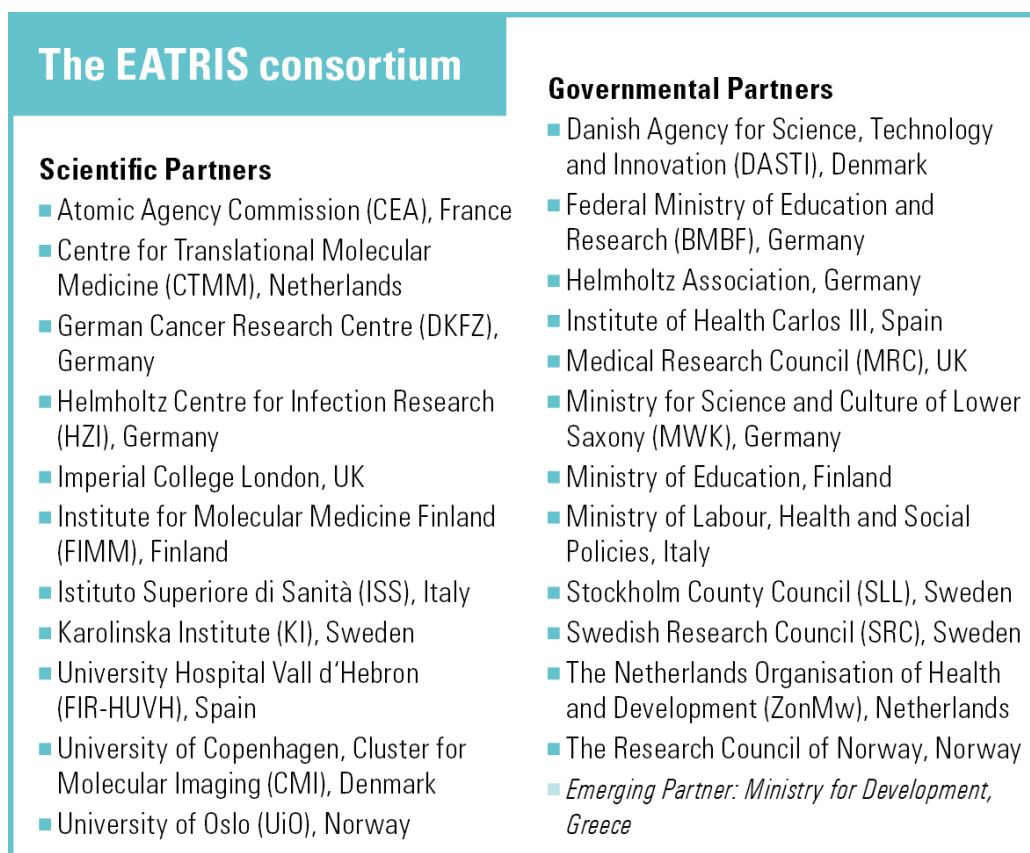
new preventive, diagnostic or therapeutic strategies at all stages of the biomedical R&D-process.

EATRIS will operate through a strong network of Translational Centres across Europe which will provide researchers with the necessary means to develop their discoveries into products. This comprises not only broad access to state of the art-facilities and technologies but also training and supporting services to optimise the outputs of both basic and clinical research. As part of its mission, EATRIS is open to everyone in the European biomedical research community. It will work together with users from academia, the public sector and industry to carry out translational projects of the highest quality standards. The primary focus of EATRIS is to serve the academic research community but it will also encourage cooperations between academia and industry.

Currently 10 European countries are partners in the EATRIS consortium (see Figure 6):

Denmark, Finland, France, Germany, Norway, the Netherlands, Italy, Spain, Sweden and the UK. Every country is represented politically and scientifically. The “Governmental Partner” represents the translational research funding policy of the country while the “Scientific Partner” represents the translational biomedical research community in the country.

The EATRIS proposal was selected by the European Commission and granted 4.2 Mio€ for a 3 years funding of the Preparatory Phase. EATRIS is still in this development phase. At the end of 2010 it will enter the implementation phase during which, the different EATRIS sites will initiate first-user projects to phase in the operation and gradually expand their capacities leading to the establishment of a full coverage of the necessary technological facilities. By 2016, EATRIS will be fully operational and offer support on a regular basis. It will be an innovation core for new diagnostics and therapies, for both researchers and industry.



**Figure 6:** The EATRIS consortium

### 1. Name and descriptive title

## EATRIS - European Advanced Translational Research Infrastructure in Medicine

### 2. Short description of new RI or major upgrade and main characteristics

There have been various activities in different European countries to improve translational research. But setting up the infrastructure required for coping with a wide range of different diseases and a broad spectrum of required treatments cannot be successfully covered by any individual country alone. This undertaking needs a truly European effort: In EATRIS ten European governments gathered to build up a distributed pan-European infrastructure based on existing biomedical translation research centres or hospitals. The aim of EATRIS is to support a faster and more efficient translation of research findings into the development of innovative strategies for the prevention, diagnosis and treatment of diseases by facilitating access to this new infrastructure. EATRIS will initially cover the following five **disease areas** that are of particular relevance for European Member States and that have a high medical and economic burden: cancer, metabolic diseases, neurological disorders, cardiovascular diseases and infectious diseases.

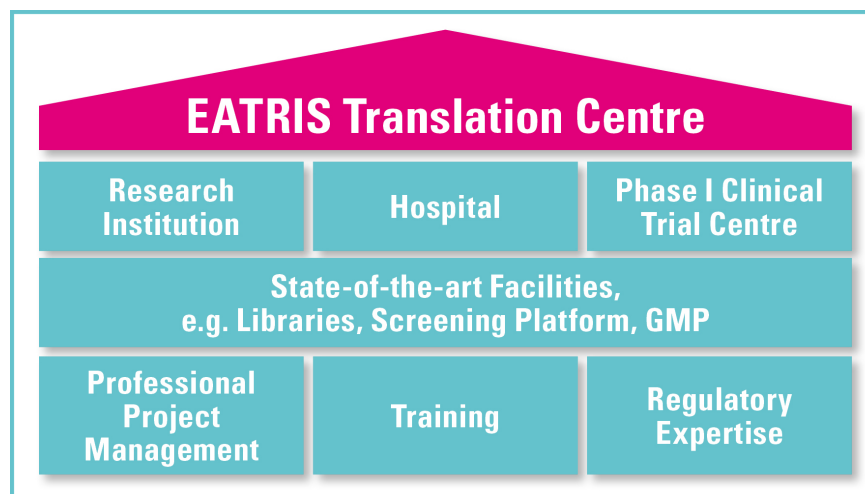
#### The EATRIS Translational Centres

At the core of the EATRIS infrastructure are the EATRIS Translation Centres organised in a pan-European network. Each Centre consists of one or more European biomedical research and development institution(s) with translational knowledge and experience, which dedicate part of their capacities (up-graded or *de novo*) to EATRIS. The goal is to have all necessary disciplines (basic and clinic research) close together as a strong innovation core. Connecting different disciplines will enhance cross-fertilisation and the creation of new knowledge. According to their core expertise the EATRIS Translation Centres will specialise in products such as diagnostics, small molecule drugs, biologics, vaccines or advanced therapy medicinal products like cell therapies.

The EATRIS Centres comprise Research Infrastructure required along the entire development chain for prevention, diagnostic and therapy for particular diseases. They combine **high-quality physical resources** (so-called „bricks“) and **scientific expertise** as well as **professional project management** („brains“). EATRIS will use the **unique approach of opening the doors** of its comprehensive Centres to provide access for external users with promising discoveries. This „brick and brains“-infrastructure will guide the scientist best through the difficult process of translational medicine.

The available infrastructure within an EATRIS Centre (see Figure 7) will consist of all facilities necessary from a **first validation** of the hypothesis (**proof of principle**) to a **proof of concept** in human (phase I/IIa clinical studies) including physical components such as

- State of the art **animal facilities** for preclinical validation studies
- **Small molecule screening facilities** to identify and characterize new drug targets
- **Compound libraries**
- **High-resolution imaging facilities** for preclinical and clinical validation
- **Cyclotrons** to produce **tracers for diagnostics and efficient therapy development**
- **“-omics” screening facilities for biomarkers and individualised medicine**
- Disease specific **patient and population cohorts** to develop and validate new hypotheses for innovative diagnostic and therapeutic strategies
- **Centralized GMP facilities** for bioprocess development and manufacturing
- Facilities to carry out **clinical phase I studies**.

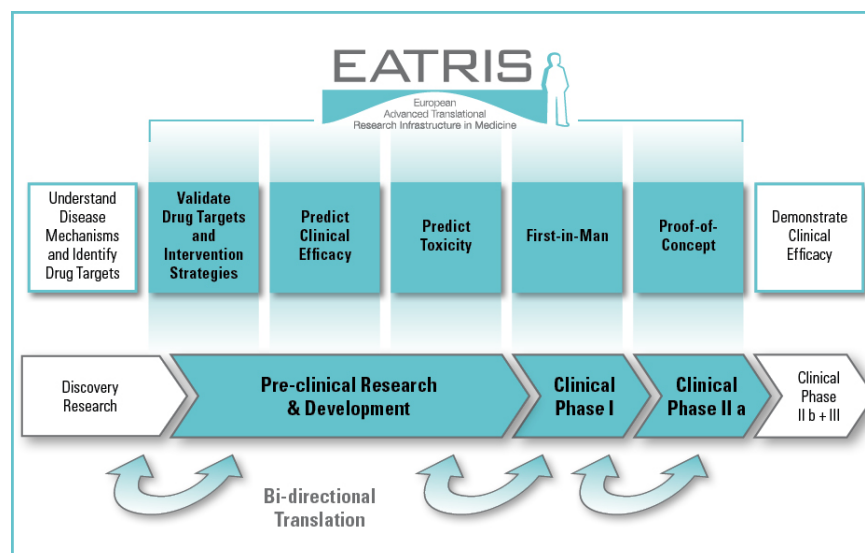


**Figure 7:** Comprehensiveness of EATRIS Translation Centres

In the same way, expertises will be part of the infrastructure such as

- Professional product research and development
- Multidisciplinary teams to accompany the development
- Regulatory knowledge
- Training programmes

For improving Europe's translational research **excellent "Brains", meaning highly qualified staff, are as essential as excellent "Bricks"**. Therefore EATRIS will offer **training and education for scientists**, physicians and nurses, technicians and science-oriented clinicians. Along with know-how and experience EATRIS will foster a philosophy of multidisciplinary exchange in its training and education of future translational research scientists. This leads to highly educated, experienced personnel and a better communication through all disciplines and all steps of the drug development chain (see Figure 8).



**Figure 8:** The developmental chain is the sequence of R&D steps for product development of clinical application in diagnosis, therapy or prevention. EATRIS will cover the steps highlighted in blue

**EATRIS will act as a motor for translational research in Europe**, by gathering translational excellence and know-how, creating new knowledge and securing critical mass of state of the art research facilities and experienced staff. The European research community as well as the health industry and public health will benefit from this effort. EATRIS will help to maximise Europe's innovative and competitive position in the global health market.

### 3. Scientific Case

The enormous progress made in biomedical research during the last two decades bears a tremendous medical and economic potential. Exploiting this potential however has been much more difficult than expected. **Translation of basic research discoveries into clinical application has turned out to be a major challenge for the European Research Area.** EATRIS is purposefully designed to help overcome the obstacles faced by academic research when translating results from bench to bedside or feeding back information from clinical application to basic research.

One major bottleneck is the **fragmented nature of science** along the development chain. There is a lack of exchange between various disciplines due to a separation of daily routine and often even the physical separation of clinical and basic research. At the start of a research project awareness of the requirements of later stages of development rarely exists since academic research is often focused on a particular aspect. Furthermore, the education and training of scientists is often too narrow and rarely bridges across the biological, medical and technical sciences.

The EATRIS translational Research Infrastructure will overcome fragmentation by establishing **multidisciplinary teams to accompany projects run within EATRIS**. These teams bring together all clinical, scientific, regulatory and product development related aspects needed over the course of the project. This helps ensure that all steps of the development process are considered from the start. EATRIS will foster a philosophy of multidisciplinary exchange in its training and education of future translational research scientists. Dedicated **training programmes** and teaching tools will be made available in all EATRIS Centres.

Translational research needs a **certain critical mass to allow for sufficient quality of procedures**. As biomedical translation is multidisciplinary by nature, critical mass is important not only at the individual company/institutional level but also at the cluster level. Many academic users suffer from the **limited availability of platform technologies** and testing facilities such as compound screening, labs and tools for validation and optimisation of therapeutic approaches. EATRIS will help secure the critical mass needed for successful translational research by creating European wide clusters for translational research. In essence, all aspects of the clinical environment and technology platforms necessary to achieve successful product development will be brought together under the EATRIS roof and be made available to all EATRIS users. These comprehensive research facilities will benefit from strong regional mobilisation.

**Access to high quality clinical data** as well as to well-defined patient cohorts is fundamental for successful translation. Access is usually limited to the research hospitals that initiated those cohorts as well as to their collaborating partners. Furthermore, there is lack of knowledge of the comprehensive regulatory requirements that have to be fulfilled for the successful transition from bench to clinical application.

**Exchange of information and knowledge** between researchers is currently often restricted to conference papers, publications and e-mail between authors. More effective collaboration during the course of research may be achieved by establishing more sophisticated exchange mechanisms. Another challenge for knowledge exchange is the overwhelming volume of data, the diversity of data and the multitude of data sources. And finally each research community or discipline has its own scientific jargon. EATRIS will help facilitate the technical, semantic and process interoperability between research sites.

The **collaboration between academia and industry** is limited in Europe, too. The traditionally strict separation of both creates hurdles in the development pathway and often means that the translation from scientific discovery to marketable product and revenue generation is more time-consuming than necessary.

EATRIS encourages **public-private cooperation** by facilitating the integration of industry with academia and encouraging a two-way exchange of resources and expertise. By offering common projects and exchange platforms to researchers in academia and industry alike, it will encourage closer collaboration.

**In summary EATRIS will improve the conditions for and the performance of translational research by**

- providing easier access to research & development facilities and translational knowhow for all scientists and researchers
- overcoming fragmentation along the translational research pathway
- fostering knowledge exchange and standardisation
- providing training programmes for the next generation of translational researchers
- facilitating and encouraging cooperation between academia and industry

#### **4. Concept Case**

The users of the EATRIS infrastructure will be basic biomedical researchers and clinical scientists located at universities, research institutions or SMEs and industrial partners that need support in order to overcome specific bottlenecks and to move their research projects from a discovery to the preclinical and clinical stage. EATRIS offers **comprehensive services to help secure the successful and rapid development of new products**. From the beginning, a translational project within EATRIS is accompanied by a multidisciplinary team and a project manager experienced in drug development and regulatory issues will guide the whole process. The guidance and support will include an assessment of the scientific basis, issues related to intellectual property rights, regulatory requirements, benchmarking with regard to existing technologies, potential risks, market potential, cost, medical need and ethical issues. EATRIS will also support the transfer of results to industry for further development.

EATRIS aims to build up an efficient national coordination to integrate existing facilities which could contribute to the infrastructure and to respond to national or regional demands. Supra-regional infrastructure which does not have to be provided locally will complement the range of services. This is supposed to create the best possible synergy in medical translational research.

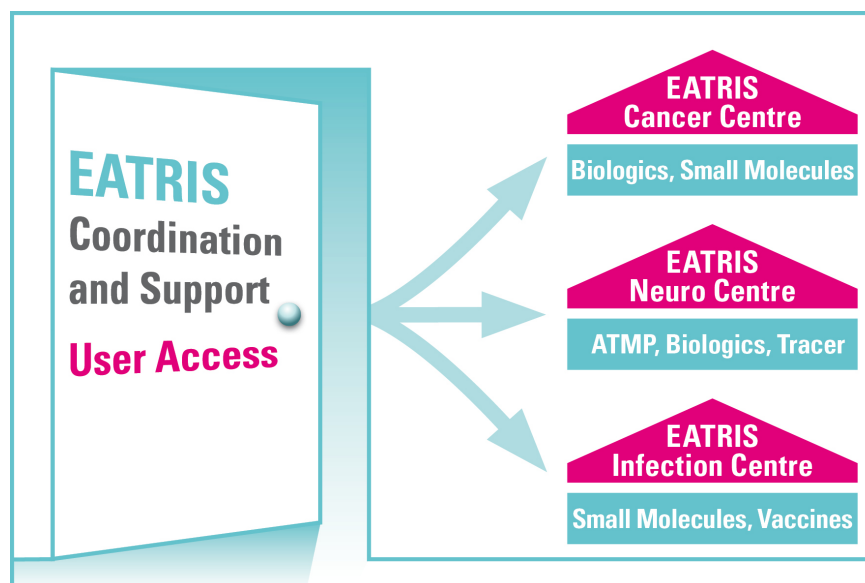
#### **Alignment of EATRIS Centres following diseases and product development**

EATRIS introduces a disease-oriented approach to provide specific knowledge and understanding of diseases needed for research in this field, to build up relevant patient cohorts and to adapt the infrastructure following the specific needs of the disease. **The translational research areas of focus for EATRIS Centres are based on product types as well as disease area**. Mostly the type of product to be developed determines the facilities needed in the EATRIS Centre. For each product, the R&D process has been analysed and the bottlenecks identified which provide obstacles to academia when wanting to develop their research into products.

#### **EATRIS acts as one**

Although EATRIS consists of many institutes throughout Europe it acts as one: The supply of research support by EATRIS is harmonised, communication and data exchange is standardised. The facilities for research are largely complementary and reach critical mass.

A central management structure “EATRIS Coordination & Support” (see Figure 9), will take care of quality management and technology transfer and will serve as an entrance portal for external scientists and industry (“one door”).



**Figure 9:** Each Centre specialises according to their disease-product-focus. The central management “EATRIS Coordination and Support services” as entrance door for external scientists and industry.

#### Close links to industry

A crucial aspect is close interaction with industry. EATRIS will establish an Industry Board to give advice and to follow-up developments in EATRIS. This will ensure a smooth and efficient commercial take-up of EATRIS products and will provide additional knowledge.

#### User Access

One of the central services offered by EATRIS is User Access, meaning that researchers across Europe can use excellent translational research resources for their already existing projects. Access criteria are:

- Proof of principle: in a first pre-clinical demonstration it must be proven that a biological process or mechanism can be targeted and potentially exploited for a new medical application.
- Scientific excellence
- Degree of innovation
- Medical need that can be addressed
- Clinical relevance / potential of becoming standard clinical practice

As part of its mission, EATRIS is open to everyone in the European biomedical research community. It will work together with users from academia, the public sector and industry to carry out translational projects of the highest quality standards. The primary focus of EATRIS is to serve the academic research community but it will strongly encourage cooperations between academia and industry.

### 5. Further information, including strategic importance to ERA

EATRIS is capable of **creating value out of basic research** by developing new medicinal products which will be commercialised by industry. The development of new medicines will change fundamentally towards a more personalized medicine. Here, EATRIS is



perfectly positioned and will serve as a valuable partner to industry.

EATRIS Centres have a high potential to become the core of **new innovation clusters** in translational research, thus providing a boost to the national economies of Member States that house them. It will help **maximise return on investment in translational research**.

The setting up of the EATRIS infrastructure will be a strategic investment to structuring the European Research Area by coordinating the existing national efforts in developing translational Research Infrastructure. EATRIS will use European synergies and the existing translational expertise to satisfy the huge demand for translational infrastructure. This will allow for better use of existing research capacity and avoidance of duplication across Europe through the bridging of complementary research facilities across the EATRIS network.

The **open access** is a crucial aspect to spread scientific excellence through Europe as a whole, as the advantages of the new infrastructure will not be limited to the EATRIS Translational, but will be open to the whole translational research community of Europe. The services will be of special importance to researchers in those countries that are facing special challenges in terms of infrastructure, economic & institutional organisation. The availability of this open infrastructure will substantially increase the attractiveness of the ERA for researchers as it increases their chances of exploiting their basic biomedical research projects. Open Access to the EATRIS infrastructure will give equal chances and thereby **strengthen the ERA**.

However the **services offered by EATRIS** in training and consulting will enable EATRIS to reach even more European Researchers. By sensitising the European medical researchers e.g. to regulatory issues EATRIS will increase the number of basic research projects that have the potential for commercial application significantly and thereby generate a powerful European research force.

By linking basic research and clinical trials and making the process from “bench to bed” more professional EATRIS will help industry to refill their pipeline with new, innovative candidates of high quality. **EATRIS “de-risks” targets for industry:** Drug candidates from academia will be more advanced on the translational path and developed following high quality standards. Industry can also benefit for their own research and development from the services as EATRIS will provide state of the art facilities and knowledge usually not available in industry like tracers and cyclotrons. This **increase in promising academic research** projects will not only **enhance the competitiveness of the EU in biomedical research** but will improve its attractiveness for the biomedical and pharmaceutical industry as well.

## **6. Identification of other socio-economic impacts**

EATRIS aims to contribute to public health by ensuring that basic research leads to new innovative medical application which will improve health. **Better health care will be possible due to faster development of new therapeutics and diagnostics.** In addition, advanced diagnostics and clinical studies aiming at patient stratification to identify non-responders will lead to a **more individualised medicine**, avoiding inefficient prescriptions and thus will allow to save costs in the healthcare system.

It will focus initially on following diseases with a major burden and unmet medical need in Europe: **cancer, cardiovascular diseases, infectious diseases, metabolic diseases and neurological diseases.** As EATRIS will not have the same economic constraints as industry, it can pursue as well rare disease areas that are not of primary interest to industry or highly innovative projects that carry a great promise but are more risky in terms of success. **EATRIS will provide the basis for a better health of the European and global population.**

EATRIS will improve the competitiveness of European research as the proximity of research and (process) development will create spin-offs. This will attract further research and business (Small and Medium Enterprises, SMEs, and big industry). The economy will improve as more



research and development will be performed in Europe. This opens the chance of more employment and due to the improved economy a higher standard of living.

### 7. Participating Members

Scientific Partner	Funding Organisations (ministries, research councils)	Associated Partners
<ul style="list-style-type: none"> <li>• Atomic Agency Commission (CEA), France</li> <li>• Centre for Translational Molecular Medicine (CTMM); The Netherlands</li> <li>• German Cancer Research Centre (DKFZ), Germany</li> <li>• Helmholtz Centre for Infection Research (HZI), Germany</li> <li>• Imperial College School of Science Technology and Medicine; UK</li> <li>• Institute for Molecular Medicine Finland (FIMM), Finland</li> <li>• Istituto Superiore di Sanità (ISS), Italy</li> <li>• University of Oslo (UiO), Norway</li> <li>• Karolinska Institute (KI), Sweden</li> <li>• University of Copenhagen, Cluster for Molecular Imaging (CMI), Denmark</li> <li>• University Hospital Vall d'Hebron (FIH-HUVH), Spain</li> </ul>	<ul style="list-style-type: none"> <li>• Federal Ministry of Education and Research (BMBF), Germany</li> <li>• Helmholtz Association, Germany</li> <li>• Institute for Health Carlos III, Spain</li> <li>• Ministry of Labour, Health and Social Policies, Italy</li> <li>• Medical Research Council (MRC), UK</li> <li>• Ministry for Science and Culture of Lower Saxony (MWK), Germany</li> <li>• Stockholm County Council (SLL), Sweden</li> <li>• Swedish Research Council (SRC), Sweden</li> <li>• The Netherlands Organisation of Health and Development (ZonMw), The Netherlands</li> </ul>	<ul style="list-style-type: none"> <li>• Danish Agency for Science, Technology and Innovation (DASTI), Denmark</li> <li>• Ministry of Education and Culture, Finland</li> <li>• The Research Council of Norway, Norway</li> </ul>

### 8. Budgetary Information

Preparatory cost	Construction cost	Operation cost (total)	Re- and decommissioning cost
<ul style="list-style-type: none"> <li>• 6 Mio €</li> </ul>	<ul style="list-style-type: none"> <li>• 20-100 Mio € per Centre (of which 80% likely be obtained by stakeholders)</li> </ul>	<ul style="list-style-type: none"> <li>• 4-8 Mio € per Centre / year (of which likely 30% be obtained by stakeholders)</li> </ul>	<ul style="list-style-type: none"> <li>• Not applicable</li> </ul>

### 9. Timetable until operation

Preparatory phase	Implementation phase	Fully operational / support on regular basis	Re- and decommissioning
2008-2010	2011-2015	from 2016	1 year

## 10. Contact

### Project Coordinator EATRIS

Prof. Dr. Rudi Balling

Director Luxembourg Centre for Systems Biomedicine (LCSB), University of Luxembourg

mail: [Rudi.Balling@uni.lu](mailto:Rudi.Balling@uni.lu)

Frank de Man, LL.M., Ph.D.

c/o ZonMW / NWO

P.O Box 93245

2509 AE Den Haag

The Netherlands

mail: [frankdeman@newyield.nl](mailto:frankdeman@newyield.nl)

phone: +31.6.53849885

### EATRIS Project Management

Helmholtz Centre for Infection Research (HZI)

Inhoffenstr. 7, 38124 Braunschweig, Germany

mail: [eatris@helmholtz-hzi.de](mailto:eatris@helmholtz-hzi.de)

phone +49 (0) 531 6181-1004

[www.eatris.eu](http://www.eatris.eu)

## 11. Progress in the Preparatory Phase

The objective of the EATRIS Preparatory Phase is to work out a master plan for the construction and operation of a pan-European translational Research Infrastructure.

As a result a first draft business plan was presented in November 2009. The business plan brings together the work of the different work packages, describing not only the strategy for setting up EATRIS Centres as translational Research Infrastructure but also describing the first considerations on governance for EATRIS, the requirements for such Centres to build up EATRIS including the Centre internal governance and the cost structure of the infrastructure.

The further planning building on the previous work was done according to 4 strands:













- In the "Scientific Strand" the requirements for EATRIS Centres as translational infrastructure were further detailed. The specifications were worked out according to products to be developed. Task forces of experts in the field were developed which further shape the strategy. Position papers are being developed which describe the user need for the different product developments, measures of quality control and quality assurance, the outlook on future developments in the field and the European added value achieved through EATRIS in this field. This is completed by an overview of expertise and facilities already available in the planned EATRIS Centres. Derived from the position papers, product sheets are compiled specific for different stakeholders to address and test our messages with them.
- In the "Marketing Strand" the needs of users, academia and industry are further explored in direct consultations but also in stakeholder meetings. The product sheets are a major input for such consultations. The scientific offer and the procedures are discussed with representatives from industry and academia to receive information on their specific interests in EATRIS and preferred procedures. This is a feedback to the scientific and organisational planning to adapt the EATRIS concept for an optimum proposition for translational infrastructure. "Marketing Plans" will identify the position of the EATRIS Centres in the research landscape, which considers the needs of all stakeholders and develops common activities to reach and retain users.
- In the "Financial Strand" financing models were explored and based on that first propositions made to the governmental partners on financing the operation of the

infrastructure in a flexible funding model involving various stakeholders. EATRIS countries and EATRIS Centres will contribute by in-kind contributions. Further funds are planned to be gained from private sources, charities and foundations as well as industry. Contributions will be reflected in the share of value generation and corresponding remuneration. Users will have to carry their own costs, but a flexible model of user fees will allow users to participate more in the results, without making access to EATRIS prohibitive if funds for such user fees are not available. Furthermore, we are currently exploring the possibility for additional (flexible) funds on the European level to complement national contributions towards operation of infrastructures.

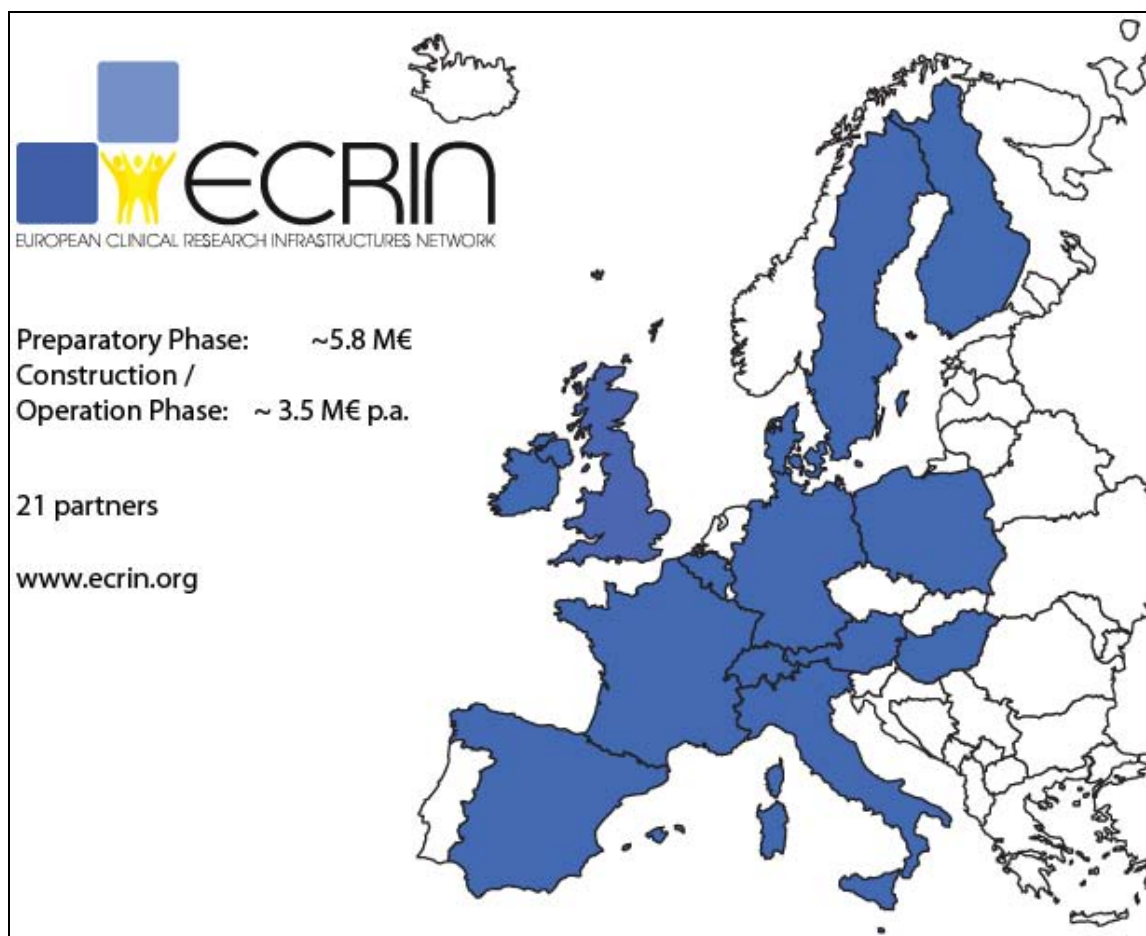
- In the “Organisational Strand” the governance and the procedures in EATRIS are planned. A Memorandum of Understanding has been signed by the countries (governmental partners) which want to follow up EATRIS and create it as legal entity.
- An Implementation Agreement is currently underway which bridges between the EC funded Preparatory Phase and the final establishment of the legal entity. During this transition period, the financing of the EATRIS management and coordination activities is ensured through the Member States of EATRIS. The agreement will be set up as close as possible to the statutes of the later legal entity. During the transition, the countries will start already the implementation of EATRIS Centres and the start of first pilot projects to demonstrate the operation of EATRIS.
- The favoured type of legal entity is the ERIC.

The Memorandum of Understanding concerning EATRIS came into force on 8<sup>th</sup> September, 2010. The future host country will be the Netherlands as elected by the EATRIS governmental partners. First commitments and financial allocations have already been made by EATRIS Member States. At the end of 2010 EATRIS will be ready for the forthcoming implementation.

**Table 5:** Links between Research Infrastructures - EATRIS

	EATRIS	Further specification of the technological link	Further specification of the thematic link	Short statement for further specification (last update February 2010)
BBMRI		Access to biological samples and defined patient cohorts. Exchange of protocols and SOP for processing of biomaterials.	Identification and verification of disease specific biomarkers, preclinical testing of new drugs and alongside clinical trial follow-up. Collaboration on ethical and legal issues in the context of biological samples & patient cohorts.	Access to biomaterials, patient groups, biobanking, ethical and legal issues
ECRIN		Access to stratified patient cohort; Exchange on best practices for preparation and conduction of clinical research projects.	Further testing of novel drugs and medicinal products in multicentric clinical trials: EATRIS and ECRIN build a continuous link from the pre-clinical and early clinical proof-of-concept (EATRIS) to the full clinical development and treatment optimisation studies (ECRIN). In this context, there will also be close collaboration on ethical and regulatory	Collaboration on clinical trial issues (multi-centre trials, cohorts but also ethical and regulatory issues) and take-up of prospective drugs from EATRIS for clinical trials from phase II onwards.
ELIXIR		e-Infrastructure for linking the numerous disparate data types that are necessary for Translational Medical Research and providing secure access where necessary	Provide data management systems to support turning biological discoveries into new medicines, vaccines and medical devices as well as collaboration on ethical, legal and standardisation issues	Provide data infrastructure, interoperability & standards.
Infrafrontier		Provision of disease-specific mouse models for efficacy tests and mouse models for safety evaluations.	Preclinical testing of novel medicinal products developed in EATRIS in suitable mouse models of INFRAFRONTIER.	EATRIS and Infrafrontier will collaborate on preclinical testing of novel drugs and treatments in mouse models for human diseases
INSTRUCT		Access to structural biology infrastructures and expertise and development of innovative approaches. Biomedical data to relate to molecular structure	Comprehensive understanding of molecular and cellular structures and function for the development of improved or novel clinical products.	Use of technologies in structural biology for toxicology, functional genomics (metabolomics), structure-activity relationship and innovation in drug development
EMBRC		Access to marine model organisms for applied sciences and novel marine-based medicines.	Harness marine biology for the development of new medicines.	Linking marine and medical research
ERINHA		Access to BSL4 Labs in the development of vaccines and anti-infectiva for risk group 4 pathogens.	Development of diagnostic, prophylactic or therapeutic drugs against risk group 4 pathogens.	Safety in the development of vaccines / anti-infectives for infectious diseases
Euro-BioImaging		Technologies for image-based verification of disease mechanisms and therapeutic strategies, exchange on innovative imaging technologies, best practices and standardized protocols for biomedical imaging.	Access to state-of-the-art imaging analysis platforms for evaluation of preclinical data and monitoring of clinical studies.	Imaging in preclinical and clinical evaluation of new diagnostics and therapies, Euro-BioImaging will provide access to imaging services and standards for methods, data, and user training to support the translational link between preclinical and clinical studies
EU-Openscreen		Bioactive compounds from the EU-OPENSOURCE repertoires will be processed to drug candidates and leads by EATRIS. On the other hand, specific assay development and verification of drug candidates / leads could be performed jointly.	Open innovation in the field of medical drug development by joint efforts in the identification and development of bioactive small molecules for clinical applications.	Drug development (Hit identification and optimisation, chemical libraries)
e-IRG		Data transfer, processing and curation.	Harmonised data management.	data processing
SSH		Novel technologies for treatments or diagnostics with influence on life style and social factors, socioeconomic impact or ethical considerations.	Ethics in diagnostics, treatment and health research	novel / improved therapies, socioeconomic impact (life quality, healthcare costs), ethics
ESP		Innovative technologies for imaging or regenerative medicine.	Fostering personalized medicine.	Imaging technologies, ATMP (regenerative medicine – synthetic biomaterials)
ENV		New technologies and methodologies to predict toxicity	Influence of substances and environmental conditions on health	Interaction between health and environment
ENE				

#### 4.5.3 European Clinical Research Infrastructures Network (ECRIN)



The European Clinical Research Infrastructures Network (ECRIN) is designed to support clinical research in Europe through consulting and services to investigators and sponsors, pending acceptance by its scientific board.

ECRIN currently covers 14 countries, representing more than 350 millions EU citizens, and plans pan-European expansion based on defined criteria (a nationwide network with a single hub acting as contact point and hosting the European correspondent). A capacity building programme allows identification of possible bottlenecks to multinational collaboration,

and develops solutions based on exchange of know-how using short term mobility.

ECRIN also plays through a portfolio of related projects a structuring role in national and European clinical research, with an active involvement in the debate on the EU legislative framework (FP7 ICREL project, [www.efgcp.be/icrel](http://www.efgcp.be/icrel)), through the support to cross-border connection of disease-oriented investigators networks (FP7 ENBREC, [www.enbrec.eu](http://www.enbrec.eu)), or the development of a strategy and tools for pan-European training programme in the field of drug development (IMI EMTRAIN project, [www.emtrain.eu](http://www.emtrain.eu)).



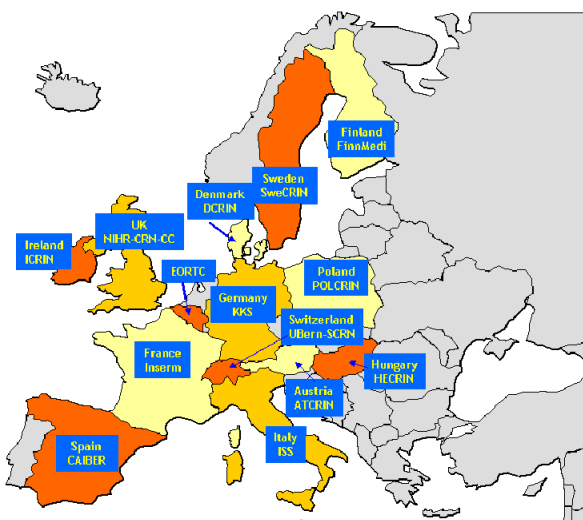
## ECRIN - European Clinical Research Infrastructures Network

ECRIN (European Clinical Research Infrastructures Network, [www.ecrin.org](http://www.ecrin.org)) is designed to provide a European not-for-profit platform for the support to pan-European clinical research projects. ECRIN is based on the connection of national networks of clinical research centres (CRC) and clinical trial units (CTU). Participants are currently Austria, Denmark, Finland, France, Germany, Hungary, Ireland, Italy, Poland, Spain, Sweden, Switzerland, the United Kingdom, and the EORTC. ECRIN provides, through a network of specialized staff hosted by each national hub and supported by their national coordination:

- **consulting** (information on regulatory and ethical requirements, on clinical trials sites and participants recruitment, on insurance, on costs evaluation and funding opportunities, on contracting and consultancy on protocol design and methodology, systematic review, meta analysis and trial sequential analysis);
- and **services** during the conduct of the study (submission and interaction with competent authorities and ethics committees, support with insurance contracting, adverse event reporting, monitoring, data management, project management, training of study personnel, investigational medicinal product management, blood and tissue management) once the protocol is accepted by the ECRIN scientific board.

Taking advantage of the know-how accumulated during the two previous FP6-funded projects (2004 and 2006), it was planned to start running a few “pilot” multinational clinical research projects to assess the organisation and procedures. ECRIN has appointed its independent **scientific board**, defined the criteria and a two-step procedure for eligibility and acceptance of projects. Currently, the scientific board secretariat receives about two new projects per month for assessment of eligibility, and the first accepted projects have started with the support of ECRIN services.

**Participants** are the **national coordination** of clinical Research Infrastructures, and national **ministries and funding agencies** in order to reach an agreement ensuring the long-term sustainability of the infrastructure (see Figure 10).



**Figure 10: Participants in the ECRIN consortium**

### 3. Scientific Case

Clinical research refers to biomedical research performed in humans. It covers a wide range of activities from randomized clinical trials on medicines, devices and other therapeutic procedures (surgery, radiotherapy), studies evaluating biomarkers and diagnostic procedures, studies on the mechanisms of disease including genetic studies, and epidemiological studies. Multinational clinical research is currently hampered by the fragmentation of health and legislative systems in Europe, making it very difficult to run investigator-driven clinical research across the borders. Industry, and particularly biotechnology and medical device SMEs, faces similar obstacles. ECRIN unlocks latent scientific potential and access to patients, thus strengthening the competitiveness of Europe in clinical science and its attractiveness for the development of preventive, diagnostic and therapeutic procedures. This is of particular importance for rare diseases, paediatrics and personalised treatments, for the development of biotherapy, for genome-wide studies requiring thousands of subjects, as well as for large clinical trials that are pivotal instruments for evidence-based medicine.

### 4. Concept Case

The ECRIN consortium is designed to provide a European not-for-profit platform for the support to pan-European clinical research projects. ECRIN connects **national hubs** coordinating networks of clinical research centres (CRC) and clinical trial units (CTU), acting in any medical field. Closely associated with scientific associations and investigators, interacting with disease-oriented investigators' networks, these national partners have the capacity to enroll patients in a wide range of clinical studies, including in rare diseases, orphan drugs, paediatrics, and biotherapy.

National networks participating in ECRIN currently cover 14 EU countries representing more than 350 million citizens. They reach the critical mass both at their country level and at the EU level. No equivalent infrastructure exists in Europe. ECRIN is not directed towards a specific specialty or disease category, but fosters transfer of best research practice from specialty to specialty all over Europe. ECRIN progressively expands to throughout the EU and associated countries, with the support of a capacity building programme facilitating the structuring of national networks and hubs.

ECRIN acts as an infrastructure providing consultation and services through a network of specialized ECRIN staff hosted by each national hub, and supported by their national network. **Information and consulting** are provided during the preparation of the study. In turn, **services** are provided during the conduct of the study, once the protocol is accepted by the scientific board.

**Consultancy and practical information during the preparation of the clinical research project includes:**

- Consultancy on protocol design and methodology
- Consultancy on systematic review, meta analysis, and trial sequential analysis
- Information on project registration
- Information on regulatory and ethical requirements
- Information on clinical trial sites and participant recruitment
- Information on insurance
- Information on cost evaluation and funding opportunities
- Information on contracting

**Services (following a task delegation contract) provided during the conduct of the clinical research project include:**

- Submission to and interaction with competent authorities and ethics committees



- Support with insurance contracting
- Adverse event reporting
- Monitoring
- Data management
- Project management
- Development of central documents and trial master file
- Recruitment and evaluation of trial sites
- Training of study personnel
- Investigational medicinal product management
- Blood and tissue samples management

Provision of consultancy and services is coordinated by the ECRIN European correspondent in the country hosting the principal investigator and/or the sponsor of the study.

ECRIN also harmonises training, tools and practice with high quality standards, fosters transparency and sharing of data and promotes collaborative projects. It also contributes to the structuring of national infrastructures, promotes a harmonised regulatory system and shared ethical standards and promotes mechanisms for funding multinational clinical research projects.

**Users** are investigators and sponsors in both the academic and industry sector, and services provided by this infrastructure are particularly relevant for research on rare diseases, for academic clinical research institutions, and for clinical trials steered by biotechnology SMEs who often lack the capacity to manufacture biotherapy products and to act as a sponsor in the conduct of EU-wide studies. Hereby ECRIN will stimulate EU research on prevention, diagnosis and treatment, hence improving healthcare delivery to patients and citizens.

#### **5. Further information, including strategic importance to ERA**

Through the **integration and harmonisation** of national clinical research capacities, ECRIN affects the scientific competitiveness of Europe in biomedical research, providing access to competence centres conducting clinical studies with high quality standards, and facilitating multinational academic clinical studies, enlarging the capacity for patients' enrolment.

This has a particular impact on translational research, allowing to best exploit the outcomes of experimental research, and in strategy studies translating clinical research into healthcare. These services are critical for or public research institutions, whose role as a single sponsor in multinational studies is made increasingly complex due to the implementation of the 2001/20/EC Directive on Clinical Trials. Industry and small and medium-sized enterprises (e.g. biotechnology and medical-device companies) will also benefit from these services.

For individual countries, participating in ECRIN provides the capacity to easily **initiate multinational clinical research projects**, therefore strengthening competitiveness and achieving leadership in clinical science, allowing for the conduct of large-scale clinical trials, genetic studies, or studies on rare diseases and personalised treatments. It also allows easy collaboration in clinical studies initiated in other countries. It fosters the participation in the portfolio of research projects ECRIN is involved in, providing facilitated access to **multinational funding** of clinical research projects, particularly through IMI and FP7 applications where cooperative clinical research now receives a substantial support.

Participating in ECRIN also helps structuring the national clinical Research Infrastructure in line with the EU standards, tools and procedures developed by ECRIN and allow to impact on the definition of these standards, tools and procedures. For the recently connected countries, it will foster the development of professionalised clinical research centres, networks and of the sponsor's capabilities in public institutions and of a national coordinating hub.

Participating in ECRIN will also result in training the European correspondents and in providing access for all the national clinical research professionals to education programmes in multinational clinical research. It will also support the national participation in the IMI training platform ([www.emtrain.eu](http://www.emtrain.eu)) coordinated by ECRIN, as well as in the portfolio of structuring projects ECRIN is involving in.

Through the joint strategic board, close collaboration will be established with the **other EFSRI BMS** Research Infrastructures, particularly the BBMRI (Biobanks) and EATRIS (translational research) projects in order to develop synergies and avoid duplication. Fostering such collaboration will provide users with a wide range of integrated services for preclinical, clinical and biomarker development.

## 6. Identification of other socio-economic impacts

Impact on **health**: clinical studies, particularly on rare diseases, will take advantage of the EU population, allowing the EU to improve their diagnostics and treatment. In addition, large-scale clinical studies are necessary to improve diagnostic and treatment strategies, and to translate into healthcare the outcome of innovation.

Impact on **economy**: investing in biomedical research leads to a perpetual return on investment of about 40% per year. Three mechanisms account for this outstanding value, and they are particularly relevant to clinical research: development of **innovative health products**, healthcare **cost containment**, and increased **productivity** of a healthy population.

The clinical proof of concept is a prerequisite for the transfer of discovery and preventive, diagnostic or therapeutic applications (medicines, medical devices, biotherapy, vaccines, diagnostics), generating value and wealth for the public and private bodies who developed the concept when reaching the market.

Investing in independent clinical trials represents a major element in the cost containment strategy for national health services, allowing to assess the real advantage of innovative (and often expensive) tools, and to set evidence-based standards of care. More generally evidence-based medicine and assessment of diagnostic and treatment strategies through randomised trials ensures optimisation of healthcare strategies, therefore contributes to the country's health and wealth.

Finally, improved productivity of a healthy population is also a string determinant of economic growth.

ECRIN will also impact on **citizens, patients, and patients associations** through its education and communication policy on clinical research. ECRIN promotes transparency, patients' rights and safety, spreading the best practice across the EU, and organises on 20<sup>th</sup> May an annual communication event targeting patients and citizens, the International Clinical Trials Day.

## 7. Participating Members

Scientific Partners	Funding Organisations (ministries, research councils)	Associated Partners
<ul style="list-style-type: none"> <li>- INSERM, France</li> <li>- Heinrich Heine Universitaet Duesseldorf, Germany</li> </ul>	<ul style="list-style-type: none"> <li>- Bundesministerium für Bildung und Forschung, Germany</li> <li>- Health Research Board, Ireland</li> </ul>	<ul style="list-style-type: none"> <li>- EFGCP, Belgium,</li> <li>- Telematikplattform, Germany</li> <li>- Ministère de la Recherche, France</li> <li>- Ministère de la Santé, France</li> </ul>

<ul style="list-style-type: none"><li>- Consorzio Italiano per la Ricerca in Medicina, Italy</li><li>- Rigshospitalet Copenhagen, Denmark</li><li>- Istituto Mario Negri, Italy</li><li>- Hospital Clinic i Provincial Barcelona, Spain</li><li>- Karolinska University Hospital, Sweden</li><li>- Medical Research Council, Hungary</li><li>- Molecular Medicine Ireland, Ireland</li><li>- University of Leeds, UK</li><li>- EORTC, Belgium</li><li>- Medical University of Vienna, Austria</li><li>- Universitat Bern, Switzerland</li><li>- FinnMedi, Finland</li><li>- Medical University Warsaw, Poland</li></ul>	<ul style="list-style-type: none"><li>- Spanish Medicines Agency and Medical Devices, Spain</li><li>- Instituto de Salud Carlos III, Spain</li><li>- Medical Research Council, UK</li><li>- Istituto Superiore di Sanita, Italy</li></ul>	<ul style="list-style-type: none"><li>- Agency for Science, Technology and Innovation, Denmark</li><li>- Science Foundation of Ireland,</li><li>- Department of Health, UK</li><li>- Ministry of social affairs and health, Finland</li><li>- Bundesministerium für Wissenschaft und Forschung, Austria</li><li>- Vinnova, Sweden</li><li>- Ministerio de Educacion y Ciencia, Spain</li><li>- Federal Science Policy Office, Belgium</li><li>- TEKES, Finland</li></ul>	
<b>8. Budgetary Information</b>			
Preparatory cost:  5.8 Mio €		Construction / Operation cost:  3.5 Mio € / year (EU correspondents, coordination)	Re- and decommissioning cost (total in Mio €)  Not applicable
<b>9. Timetable until operation</b>			
Preparatory phase  2008-2011		Construction / Operation  From 2011	Re- and decommissioning
<b>10. Contact</b>			
Project coordinator: Jacques Demotes-Mainard INSERM – Institut de Santé Publique 101 rue de Tolbiac, 75654 PARIS cedex 13 <a href="mailto:jacques.demotes@inserm.fr">jacques.demotes@inserm.fr</a> , tel +33 1 44 23 62 85 <a href="http://www.ecrin.org">www.ecrin.org</a>			

## 11. Progress in the Preparatory Phase

The ECRIN Preparatory Phase aims to develop a sustainable infrastructure able to support the set-up, conduct and analysis of multinational clinical projects in Europe. The work plan was broken down into 11 work packages (see Table 6).

To date, a new governance structure was implemented with a project development board composed of scientific partners, ministries and funding agencies, in charge of supervising the discussion on the legal status and on the financial management. The decision to apply for an ECRIN-ERIC statute was agreed by the ECRIN network committee and the final version of ECRIN-ERIC statutes, the business plan and technical annex are available.

The EU funding helped to hire in each country a European correspondent in charge both of structuring activities and of the local coordination of operations. Taking advantage of the knowledge accumulated during the previous steps, the education programme started with two summer schools devoted to the training of European correspondents.

A strategy was developed for the capacity building programme with a diagnostic step followed by support measures, in order to strengthen the structuring of new national networks, thus facilitating the extension to additional countries. A new country, Poland, was accepted as a new partner in the initiative by the ECRIN network committee.

The communication strategy targeted patients and citizens, investigators and sponsors, disease-oriented networks and policy makers.

Specifications for certification of data centres were prepared and a call for ECRIN data centres will be launched, taking into account those specifications.

The existing GMP facilities for biopharmaceuticals and biotherapy were inventoried.

National and pan-European strategies for provisions of support to clinical research projects were further defined and an appropriate quality assurance system was developed.

An independent scientific board was nominated, and a first set of criteria and procedures for eligibility and acceptance was implemented. Currently, the scientific board receives about two new projects per month for assessment, the first accepted projects started with the support of ECRIN, and others will follow soon.

**Table 6:** Overview of the several work packages of ECRIN

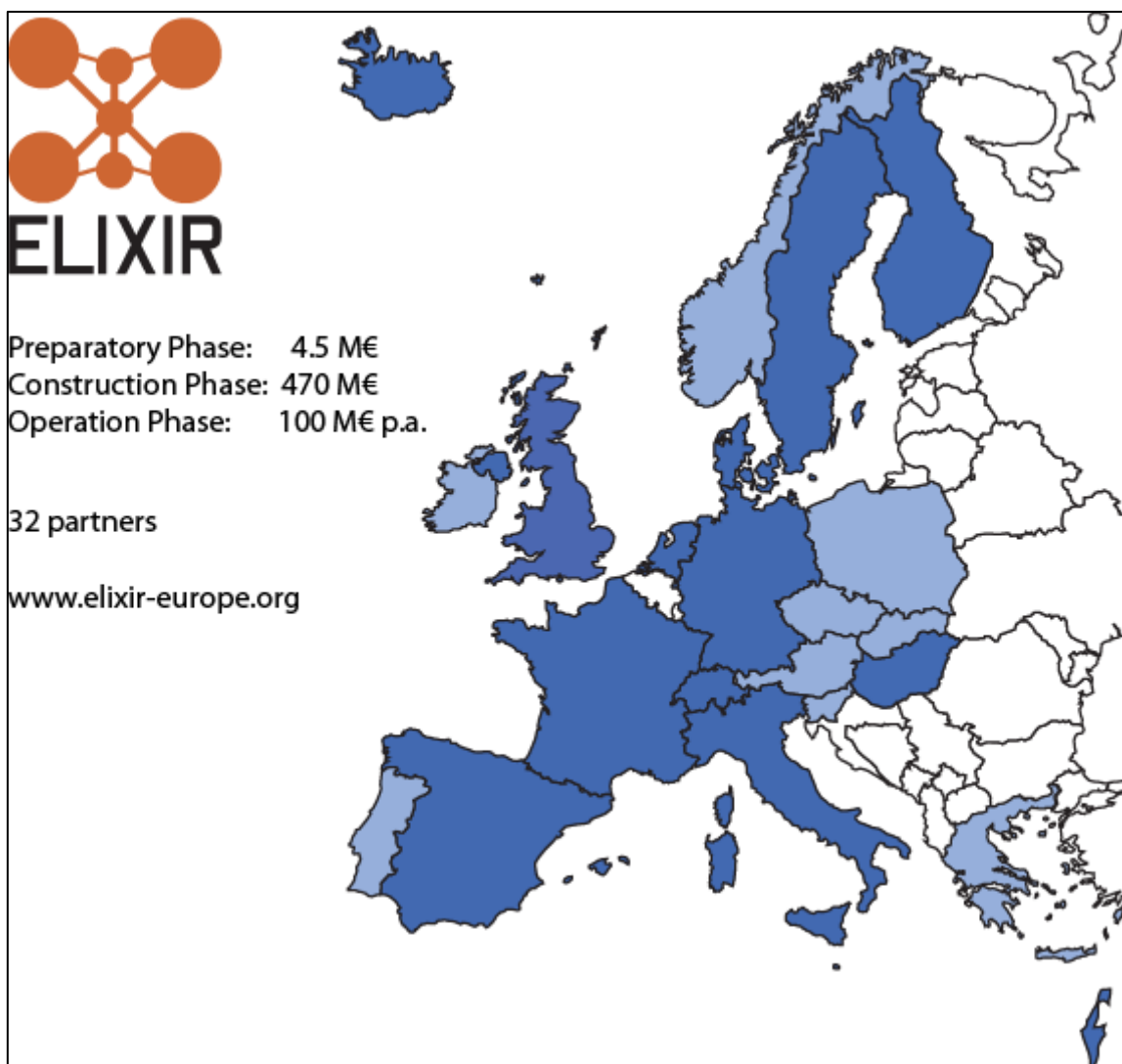
	M3	M6	M9	M12	M15	M18	M21	M24	M27	M30	M33	M36
<b>WP1. Management</b>												
Management of the grant agreement												
Management of the overall strategy												
<b>WP2. Legal status and governance</b>												
Agreement on the governance												
Implementation of the governance												
Agreement on legal status												
Implementation of status												
<b>WP3. Financial plan</b>												
Surveys												
Evaluation of the costs												
Contract on the business plan												

93

**Table 7:** Links between Research Infrastructures – ECRIN

	ECRIN	Further specification of the technological link	Further specification of the thematic link	Short statement for further specification (last update September 2010)
BBMRI	↔	Common procedures for biobanking of clinical samples	Harmonisation of ethical and legal framework for clinical research and biobanking. Development of pan-European strategy and shared tools for education and training programme (IMI/ www.emtrain.eu)	
EATRIS	↔	Clinical development of translational research outcomes	Development of pan-European strategy and shared tools for education and training programme (IMI/ www.emtrain.eu)	
ELIXIR	↔	Tools for data management, storage and analysis	Development of pan-European strategy and shared tools for education and training programme (IMI/ www.emtrain.eu)	
Infrafrontier	↔	Access to data on animal models and phenotyping techniques useful for clinical research development, and development of phenotyping methods in line with the relevant clinical endpoints.	Development of pan-European strategy and shared tools for education and training programme (IMI/ www. emtrain.eu)	
INSTRUCT	↔	Access to biomedical data, and use of protein structure to predict efficacy and safety of drugs	Development of pan-European strategy and shared tools for education and training programme (IMI/ www. emtrain.eu)	
EMBRC				
ERINHA	↗		Potential clinical test development	
Euro-BioImaging	↔	Common imaging standards	Clinical studies for evidence based diagnosis	
EU-Openscreen	↗		Potential medical drug development	
e-IWG				
SSH				
ESP				
ENV				
ENE				

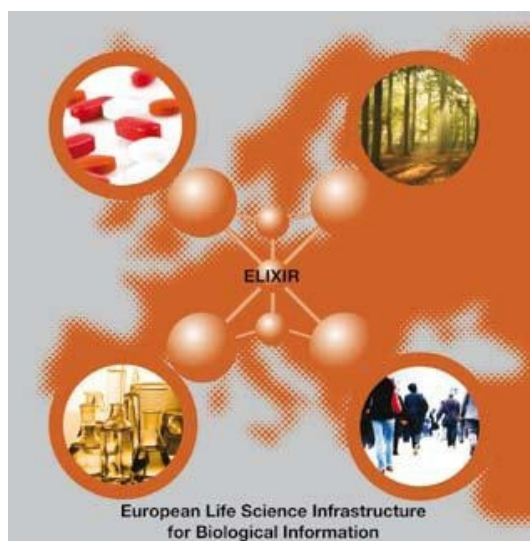
#### 4.5.4 European Life-science Infrastructure for Biological Information (ELIXIR)



ELIXIR will permit the integration and interoperability of huge amounts of diverse, heterogeneous information that is essential to generate and utilise biological knowledge. It will encompass the necessary major computer infrastructure to store and organise this data, removing redundancy, in a way suitable for rapid search and access, and will provide a sophisticated and user-friendly portal for users.

It will facilitate the European component of the major international collaborations that

collect, curate and annotate biological information world-wide. It will develop processes for (i) managing the integration of novel data-types, (ii) supporting for interoperability of analytical tools (although it will not support the development of the tools themselves, except in the very limited case where the tools are necessary for the ELIXIR core mission) and (iii) developing standards and ontology for biological information and encourage their widespread adoption (see Figure 11).



**Figure 11:** Interactions within the European Life-science Infrastructure for Biological Information ELIXIR

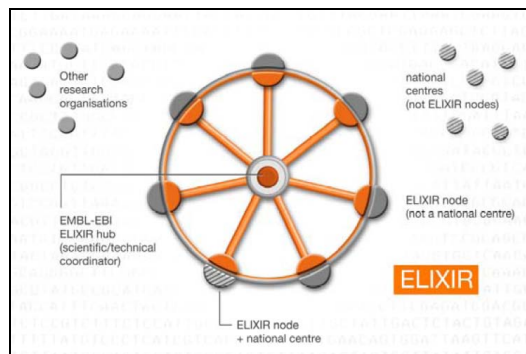
ELIXIR has the largest user community of any of the ESFRI Research Infrastructures, potentially many millions. For this reason, consultation with the user community and other stakeholders has been the major activity of the first part of the Preparatory Phase. This process was managed through work package 3 and was targeted at the four major sectors of our community; industrial users of the data, academic and clinical users of the data, large scale data providers and our international collaborators.

The formal part of the ELIXIR user and other stakeholder consultation has been completed. The reports and other outputs from the work packages, feasibility studies, stakeholder meetings, surveys and Member State visits are all on the ELIXIR web site. The ELIXIR steering committee will continue to operate for the remainder of the Preparatory Phase and will continue to consult the stakeholders as and when necessary.

The scientific and technical aspects of ELIXIR are relatively uncontroversial and there is widespread agreement on what is required. The steering committee has thus spent the greater part of its efforts dealing with organisational and funding matters.

We have identified a hub and spoke structure (see Figure 12) as the only realistic structure for ELIXIR. The hub will be located

at EMBL-EBI in the UK, it will continue to host the core data-collections and the ELIXIR secretariat, it will manage the ELIXIR European data centre, it will represent Europe in the international data collaborations and it will coordinate the nodes.



**Figure 12:** Hub and spoke structure of ELIXIR

Nodes will host components of the European infrastructure and will be configured so that they can interoperate both with the central hub and with each other. Nodes will be located in the Member States and will be funded by them.

A country may have more than one node, some countries may wish to pool resources to create regional nodes and nodes may also be virtually. Nodes will need to be able to enter into a binding agreement with the hub and will need to have sustainable funding. In spring 2010 a „request for suggestions for ELIXIR nodes“ was launched, nearly 50 suggestions were received from 20 countries (see Figure 13). As was envisaged, a number of different kinds of nodes were received, including scientific nodes that host data collections and related services, compute nodes that provide significant computational resources and service nodes that provide functions such as training, standards development and benchmarking.

On the face of it ELIXIR would appear to be considerably ahead of the timetable as two countries (Sweden and the UK) have already committed funds to ELIXIR by the end of 2009, something that was not envisaged as happening until after the end of the Preparatory Phase (press releases describing these investments are available from the ELIXIR website.) This has allowed



us to start construction much earlier than anticipated and the £10 Mio investment from the UK is being used to initiate the implementation of the ELIXIR European data centre.



**Figure 13:** Map of distributed ELIXIR partners in Europe

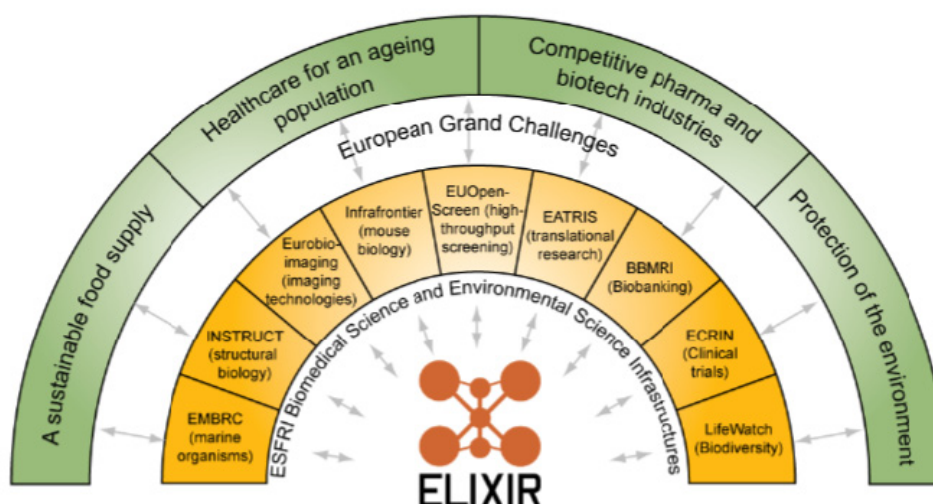
There remains, however, the problem of funding the hub. The hub will be responsible for a substantial task and we estimate that it will need 50% of ELIXIR funds in order to achieve this. As at the time of writing, no country has made any indication that it will be prepared to contribute to the core costs. Finding an optimal solution to this problem is

a significant challenge and critical for the whole infrastructure to succeed.

This is particularly worrying since ELIXIR plays so strongly to the European Grand Challenges of 1) Healthcare for an ageing population, 2) A sustainable food supply, 3) An internationally competitive pharmaceutical and biotechnology Industry, and 4) Protection of the environment. It is widely believed that the high-throughput data-generation technologies that have come out of the Human Genome Project and related activities will contribute to solutions to these problems. Of course, this will only happen if Europe builds the necessary Infrastructure to curate, archive and make these data available to the scientific community. This is the primary role of ELIXIR.

Additionally, the ESFRI BMS and Environment RIs are, of course, a key part of this and it is a no less important role of ELIXIR to provide these RIs with the infrastructure necessary to utilise these data in a manner that is most appropriate for their users (see Figure 14).

If Europe is going to succeed in finding solutions to these challenges and to remain competitive in the life-sciences with the US, Japan and the emerging economies then a sustainable source of funding for the ELIXIR hub will need to be found.



**Figure 14:** Interactions between ELIXIR and its scientific surrounding



### **1. Name and descriptive title**

## **ELIXIR - European Life-science Infrastructure for Biological Information**

### **2. Short description of new RI or major upgrade and main characteristics**

The objective of the ELIXIR Preparatory Phase is to produce a Memorandum or Memoranda of Understanding between organisations (government agencies, research councils, funding bodies and scientific organisations) within the Member States, with the purpose of constructing a world class and globally positioned European infrastructure for the management and integration of information in the Life Sciences.

To achieve this, we will address the following tasks and issues:

- 1) Define the scope of the infrastructure, its role and benefits
- 2) Define an appropriate governance and legal structure
- 3) Define a long-term funding structure to provide a sustainable infrastructure
- 4) Define the requirements for the European data centre in the next 5-10 years and make plans to meet these needs
- 5) Involve all relevant stakeholders, including users, data providers, and tools providers to ensure that the infrastructure meets their needs
- 6) Explore integration and interoperability between core and specialised data resources and the development of standards in newly emerging fields
- 7) Define the critical interdisciplinary links that need to be forged between the „biological“ and related scientific disciplines, including medicine, agriculture and the environment
- 8) Define the needs of related European industries
- 9) Define a training strategy to ensure that Europe effectively exploits all the available information

The specific activities of the Preparatory Phase will include:

- a) Holding stakeholder meetings to bring together national representatives, key scientific opinion and funding organisations.
- b) Establishing working parties, supported by technical feasibility studies where appropriate, to address the tasks and issues above with final reports at month 20.
- c) Consolidating these reports into a management and funding proposal to be sent to Member States and funding agencies with draft MoU by month 38 to seek agreement by month 50.

### **3. Scientific Case**

A European infrastructure for biological information is needed because:

- Optimal exploitation of Life Science data is crucial to research.
- The exploitation of the flood of data promises substantial and diverse increments in well-being.
- Huge investment in science will be wasted if its output is not preserved.
- Public databases are the only way to satisfy scientific needs.
- Current European funding is inadequate.
- A unified European funding strategy is essential to minimise costs.
- Information infrastructure costs are a small fraction of the data gathering costs.
- Coordination of standards is essential to realise the composite value of the data.
- Data collections are growing exponentially.
- New high-throughput methods generate new data requirements.
- A single European voice will influence global decisions and maintain open access.
- Significant upgrades are essential to provide uninterrupted robust services.

- The already-huge user community is growing relentlessly.
- New accession states are emerging as strong contributors to and users of the information.

These challenges need to be addressed at a European (rather than national) level because the benefits are pan-European, there is a need for European coordination and it is important for European competitiveness and return on investment.

#### 4. Concept Case

The mission of this European Life Sciences information infrastructure is to construct and operate a sustainable infrastructure for biological information in Europe to support Life Science research and its translation to medicine and the environment, the bioindustries and society. This will enhance all research and industry associated with living systems including: health and medicine, the environment, the bio-industries and society.

To achieve this we will:

- Establish a trans-national infrastructure for biological information and service providers, including existing national infrastructures and networks.
- Implement a major upgrade to the current infrastructure for the core molecular information at the European Bioinformatics Institute (EMBL-EBI), including construction of a European biomolecular data centre.
- Promote the use of state of the art IT technology for data integration and database interoperability.
- Promote and further develop the use of distributed annotation technologies for large scale European collaborations in the Life Science databases.
- Promote the development of infrastructures for biological information in the new accession states.
- Develop an appropriate legal and financial framework for the construction and sustainable operation of this infrastructure.
- Promote the formation of an associated European framework for training and outreach.

This will contribute to European science by:

- Optimising access and exploitation of shared Life Science data.
- Ensuring longevity of the data and protecting investments already made in research which collected the data.
- Increasing the competence and size of the already large user community by strengthening national efforts in training and outreach.
- Enhancing the effectiveness of pan-European collaboration by improved data exchange.
- Enhancing the global success and influence of Europe in Life Science research and industry.

ELIXIR will comprise:

- An interlinked collection of „core“ and specialised biological data resources and literature.
- Standards and ontology for newly emerging data.
- A major upgrade for the core information resources at the EBI.
- New data resources as appropriate.
- Integration and interoperability of diverse heterogeneous data.
- Rapid search and access through friendly portal(s) supported by appropriate computer hardware infrastructure.
- Infrastructure linking core data resources and national bioinformatics data and service providers.

- Infrastructure to enable distributed annotations and tool development.
- The opportunity to establish infrastructures for Life Science information in the accession states.
- Links between molecular resources and developing resources for medicine (e.g. biobanks), agriculture and the environment (e.g. biodiversity).
- Access to high performance computing, through links to Europe's supercomputer centres.
- Coordination and provision of training and outreach across Europe to enhance national efforts.
- Strong links to European biindustries to ensure the optimal translation of Life Science research into the bioindustrial sector in Europe.

Funding will be needed for new data resources (e.g. chemicals in biology & medicine, metabolites, pharmaceuticals), imaging data (from cells to organisms), human variation data, ensemble for non-vertebrates, a major literature resource. Also there is little national funding for distributed specialist resources and for the hardware, software and personnel to integrate the specialist distributed resources with core resources. These latter areas will be considered and included in the ESFRI ELIXIR pan-European infrastructure.

The Preparatory Phase of ELIXIR will define the most appropriate structure for the infrastructure. There can be no definitive statement of priorities or selection at this time since this would be based on considerations made without resolution of legal, governance, strategic and financial issues.

#### **5. Further information, including strategic importance to ERA**

The anticipated impact of ELIXIR is that it will contribute technological development capacity in the European Research Area in the following ways:

- Basic world-class infrastructure to support world-class research
- Facilitate exploitation of public data
- Facilitate integration of data
- Ensure coordinated approach to establishment and support of core data resources, avoiding duplication of effort and resources
- Provide support for Life Science industries, to ensure that they are able to fully exploit available knowledge and so boost the knowledge economy
- Encourage the spread of excellence in computational biology throughout Europe, from the convergence regions to the outermost regions – with computational networks, this is now entirely possible
- Provide a coordinated training strategy across Europe to ensure all our life scientists know-how to exploit available data.
- Provide a single voice for Europe in global infrastructure consortia and decisions.
- Provide an effective training strategy for life scientists

#### **6. Identification of other socio-economic impacts**

At a general level, the catalytic effect of this initiative will result in pan-European impact, will benefit from the participation of multiple centres and multiple Member State organisations, is important for European scientific competitiveness and cannot reasonably be expected to be funded by a single Member State.

The infrastructure will capitalise on existing funding across Europe: Currently, the Member States already invest considerable sums into collecting data and bioinformatics research. It is now generally acknowledged that the data and information generated by such research must be efficiently captured electronically and made available. A Europe-wide approach to this problem will make the whole process more cost-effective and much synergy will be generated

by the integration of information across Europe.

The infrastructure builds strongly on past and current EU consortia, including networks of excellence and integrated projects. The infrastructure proposed in ELIXIR will complement (not replace) these research projects. Indeed we envisage this infrastructure supporting an extended portfolio of EC-supported and Member State supported research projects and consortia.

## 7. Participating Members

Scientific Partner	Funding Organisation
<ul style="list-style-type: none"> <li>- The Barcelona Supercomputing Centre</li> <li>- The Spanish National Cancer Research Centre</li> <li>- The Center for Advanced Studies, Research and Development in Sardinia</li> <li>- The Finnish IT center for science</li> <li>- The Center for Biological Sequence Analysis at The Danish Technical University</li> <li>- Erasmus Medical Center</li> <li>- EMBL-EBI</li> <li>- The German Research Centre for Environmental Health</li> <li>- The Hungarian Institute of Enzymology</li> <li>- Linköping University Department of Physics, Chemistry and Biology</li> <li>- Radboud University Nijmegen Medical Centre</li> <li>- The Sanger Center</li> <li>- The Swiss Institute of Bioinformatics</li> <li>- Syngenta</li> <li>- The Technical University of Braunschweig</li> <li>- The University of Bordeaux 2</li> </ul>	<ul style="list-style-type: none"> <li>- The UK Biotechnology and Biological Sciences Research Council (UK)</li> <li>- The German Federal Ministry of Education and Research (DE)</li> <li>- The Italian National Research Council Department of Life Sciences (IT)</li> <li>- The German Research Foundation (DE)</li> <li>- Genome Espana (ES)</li> <li>- The French National Institute for Research in Computer Science and Control (FR)</li> <li>- Israel Ministry of Science &amp; Technology (IL)</li> <li>- UK Medical Research Council (UK)</li> <li>- UK National Environment Research Council (UK)</li> <li>- The Netherlands Organisation for Scientific Research (NL)</li> <li>- Icelandic Center for Research (IS)</li> <li>- Sardenga Ricerche (IT)</li> <li>- The Swedish Research Council (SE)</li> <li>- The Wellcome Trust (UK)</li> <li>- The French National Institute for Agricultural Research (FR)</li> <li>- The French National Institute for Health and Medical Research (FR)</li> </ul>

## 8. Budgetary Information

Preparatory cost	Construction cost (total in Mio €)	Operation cost (total)	Re- and decommissioning cost (total in Mio €)
4.5 Mio €	470 Mio € to be further determined in pp	100 Mio € to be further determined in pp	

## 9. Timetable until operation

Preparatory phase	Construction phase	Operation	Re- and decommissioning
2007 to 2011	2011	2012 onward	

## 10. Contact

Prof. Janet Thornton, EMBL-EBI, Wellcome Trust Genome Campus, Hinxton, Cambridge, UK, CB10 1SD, UK. [www.elixir-europe.org](http://www.elixir-europe.org)

## 11. Progress in the Preparatory Phase

ELIXIR has made dramatic progress in its second year, receiving a £10 Million pulse of capital from the UK BBSRC which has allowed construction to commence much sooner than anticipated. These funds will be used to construct the first phase of the European bio-Molecular data centre. Additionally, Sweden has committed 19 Million SEK to be invested locally and a number of other countries are close to concluding similar investments. Although this is very encouraging, and means that ELIXIR is substantially ahead of its original timetable the major problem still remains that of providing long-term funding for the nodes and sufficient funds for the construction of the hub.

The steering committee has identified a distributed hub and nodes structure as the only realistic way of constructing ELIXIR for the following reasons:

- 1) The Hub will be required to hold the core datasets, take part in the international collaborations that maintain them and coordinate the nodes in order to minimise duplication and ensure that no part of the requirement is overlooked.
- 2) The task is now so large that it cannot be accomplished at a single site.
- 3) Some datasets may be so large that it will not be possible to distribute them in an ad hoc way, rather it will be necessary to manage the distribution, possibly through a series of tiers as with the data from CERN.
- 4) The level of robustness and reliability that are now needed are best delivered by holding the data and services at multiple sites.

The coordination role of the hub is particularly important as it will ensure that the nodes maintain interoperability, that all the requirements are being fulfilled and that there is no duplication and waste. The size and scope of this role is such that we anticipate that it will need 50% of the total funding for ELIXIR. If Europe is going to succeed in finding solutions to these challenges and to remain competitive in the life-sciences with the US, Japan and the emerging economies then a sustainable source of funding for the ELIXIR hub will need to be found.

The ELIXIR Preparatory Phase is organised into 14 work packages, five feasibility studies and nearly 20 committees. All of the work packages and feasibility studies have completed their work and published their findings with the exception of WP6 (physical infrastructure) which has taken on a new task, that of interacting with the e-Infrastructure projects in order to assist the ESFRI BMS initiatives with their infrastructures. A series of technical meetings and workshops will be necessary to work out what needs to be done to ensure that all of the ESFRI BMS initiatives can exchange data seamlessly and avoid duplication and waste. We anticipate that it will be necessary to set up joint working groups with the other projects and have already done this for INSTRUCT and BBMRI.

As this process is of vital importance to the success of the ESFRI BMS RIs and is also likely to be quite protracted we have requested, and been granted, a 1 year no-cost increase in the length of the Preparatory Phase in order to continue to run the ELIXIR steering committee to give oversight of this by the European bioinformatics community.

ELIXIR probably has the largest user community of any of the ESFRI Research Infrastructures, potentially many millions (for example, EMBL-EBI currently performs analyses for more than 1 Million unique users per annum). For this reason, consultation with the user community has been a major activity. WP3 (users) had three committees to manage this (bioinformatics communities, industry and data providers) and they have completed their planned

consultations. In addition, EMBL-EBI represents Europe in many international collaborations that manage the core data collections at the global level, and we have consulted our collaborators. The industry committee has taken on a new role and is continuing to meet. It will be looking at ways in which Industry could provide funds for ELIXIR. We would also like to continue to run the communities committee in order to stay in touch with the users until construction begins in earnest. We hope to achieve this through the no-cost extension.

We have completed and written up our European surveys, one for data-users and one for data-providers. These have provided invaluable data for the steering committee which is being fed into the plans for the construction phase.

The three international stakeholders meetings were well attended, generated considerable interest and provided useful guidance to the steering committee. Another reason for extending the period of the Preparatory Phase is to ensure continuity of progress, and if there are sufficient funds available we may decide to hold another stakeholders meeting during the extension.

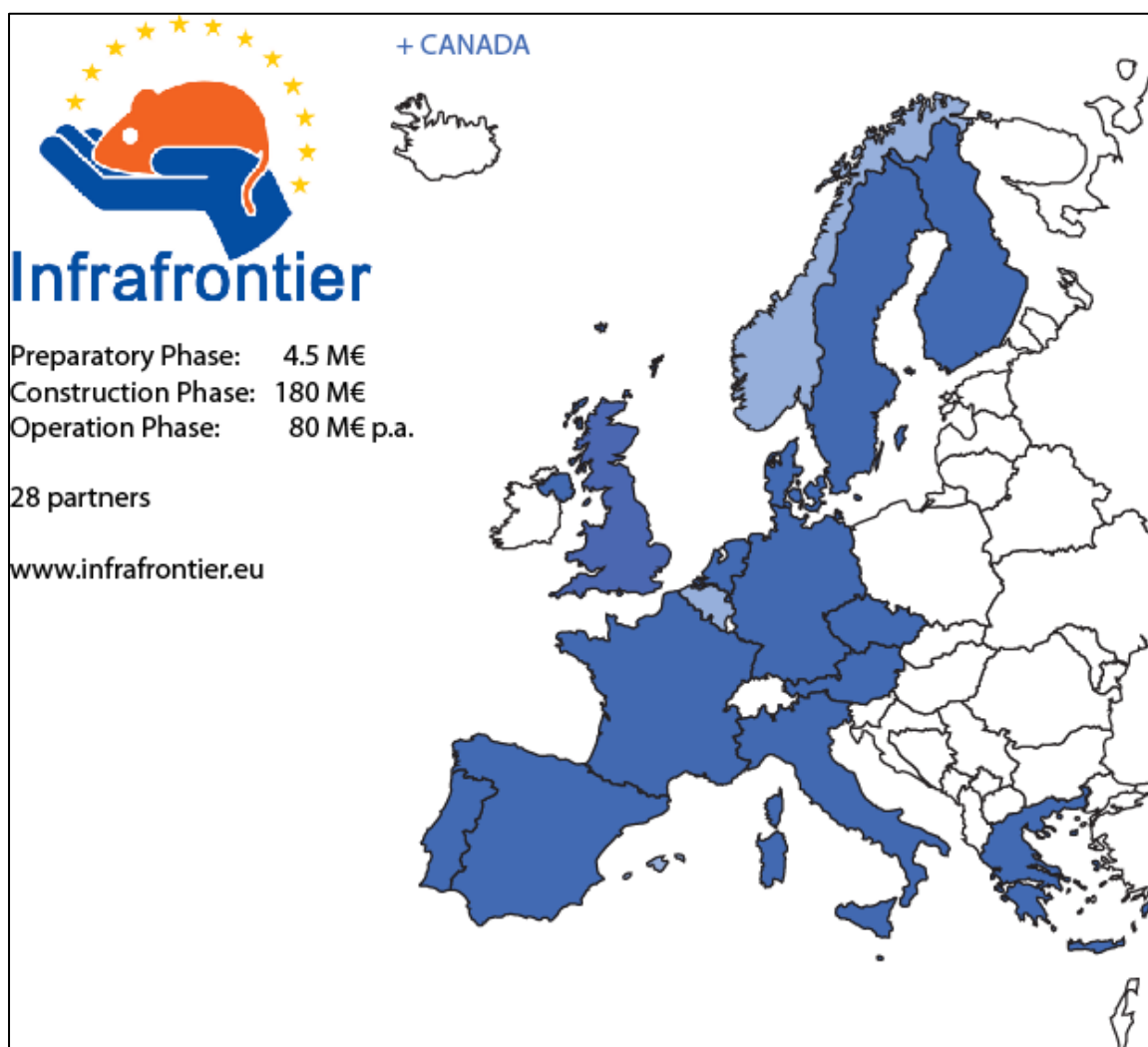


**Table 8:** Links between Research Infrastructures - ELIXIR

	ELIXIR	Further specification of the technological link	Further specification of the thematic link	Short statement for further specification (last update February 2010)
BBMRI		e-Infrastructure to enable the linking of biomolecular data to clinical, phenotypic and other data associated with sample collections	Enabling clinical research using samples collected from patients and volunteers	Provide data infrastructure, interoperability & standards.
EATRIS		e-Infrastructure for linking the numerous disparate data types that are necessary for translational medical research and providing secure access where necessary	Provide data management systems to support turning biological discoveries into new medicines, vaccines and medical devices	Provide data infrastructure, interoperability & standards.
ECRIN		e-Infrastructure to enable the linking of medical records to biomolecular data and providing access to appropriately accredited and authenticated investigators	Data management systems to allow the use of omics technologies in clinical trials and studies	Provide data infrastructure, interoperability & standards.
Infrafrontier		Make e-Infrastructure developed for the human genome available to the mouse community	Support the development and deployment of mouse models for research on human disease and other applications	Provide data infrastructure, interoperability & standards.
INSTRUCT		e-Infrastructure for the deposition, curation, annotation, archiving and publishing of biomolecular structures and related data	Enabler of structural biology, support for integration of different structure determination technologies	Provide data infrastructure, interoperability & standards.
EMBRIC		Make e-Infrastructure developed for the human genome available to the marine biology community	Enable the use of omics technologies in marine biology for environment protection and other applications	Provide data infrastructure, interoperability & standards.
ERINHA		Provide secure e-Infrastructure for handling omics and related data from category IV organisms	Enabler of research to prevent pandemics	
Euro-BiolImaging		e-Infrastructure for linking images to biomolecular data	Most areas of life sciences are starting to use imaging as a research tool. In many cases it is highly desirable to link the images to biomolecular data. ELIXIR will enable these links.	Provide data infrastructure, interoperability & standards.
EU-Openscreen		e-Infrastructure for linking biomolecular and chemical-biology data	Support public domain open access drug-discovery	Provide data infrastructure, interoperability & standards.
e-IRG				Provide requirements analysis for other biology RI, assist in deployment to other biology RI.
SSH				
ESP				
ENV		e-Infrastructure for the use of omics technologies for environmental monitoring.	Support research into climate change, environmental protection and environment monitoring	Provide data infrastructure, interoperability & standards.
ENE				

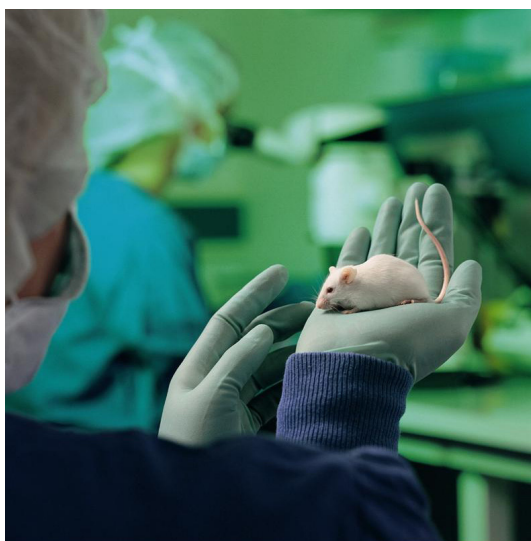


#### 4.5.5 European Infrastructure for phenotyping and archiving of model mammalian genomes (INFRAFRONTIER)



Men and mice share 95% of their genetic make-up and researchers have developed a comprehensive toolbox to study the functional effects of genetic variation in the mouse on development, morphology, physiology and metabolism. This is the reason why mice are ideal models for complex human diseases such as diabetes, osteoporosis, asthma or depression (see Figure 15).

An essential task for the biomedical sciences will be the functional analysis of every gene in the mammalian genome. Community-driven research projects and large-scale systematic mutagenesis programmes produce thousands of new disease models, but the major bottlenecks are the proper characterisation (systemic phenotyping), archiving and distribution of mouse models for the biomedical research community.



**Figure 15:** Mouse as model organism for biomedical sciences

It is clear that this tremendous task cannot be fulfilled by individual research facilities or on the national level alone. Therefore INFRAFRONTIER integrates 18 research laboratories from Europe and Canada with exceptional track records to implement and run large Research Infrastructures. Together with the 15 partners from ministries, funding agencies and research councils they develop a sustainable funding concept for INFRAFRONTIER. **Czech Republic, Austria, and Canada**, which initially participated as “observers”, became full members in 2009. Belgium and Norway have meanwhile obtained observer status.

The partners of INFRAFRONTIER use the Preparatory Phase (starting from March 2008 and funded by the European Commission with 4.5 Mio €) to tackle central issues of the emerging infrastructure such

as overall strategy and governance, legal matters, and sustainable funding. Technical questions such as generic engineering specifications for the emerging facilities and the bioinformatics required to manage the data are also being addressed. Other important issues are the transfer of know-how between existing and new facilities, and the involvement of additional partners, particularly from the new Member States of the EU.

In June 2010 the business plan and the statutes of the **INFRAFRONTIER legal entity** have been discussed at the annual meeting. Scientific and funding partners agreed on the proposed implementation strategy. A funders meeting in autumn 2010 and the establishment of a dedicated Inter-Ministry working groups will be the next steps in the implementation process of the pan-European INFRAFRONTIER Research Infrastructure.

INFRAFRONTIER has established close connections with the other BMS Research Infrastructures. Examples are thematic workshops on common aspects of the Preparatory Phase such as the assessment of the available legal forms, a joint effort of the BMS Research Infrastructures to establish a European medicines research training network (EMTRAIN) together with partners from the pharmaceutical industry in the context of the Innovative Medicines Initiative (IMI), the identification of common e-infrastructure requirements or joint outreach activities. Scientific cooperation with BMS Research Infrastructures will create further synergies during the implementation phase of INFRAFRONTIER.

### 1. Name and descriptive title

## INFRAFRONTIER – European Infrastructure for phenotyping and archiving of model mammalian genomes

### 2. Short description of new RI or major upgrade and main characteristics

The fields of functional genomics, medically related Life Sciences and systems biology use the mouse as a model system to understand the molecular basis of health and disease in man. In the coming decade, saturation mutagenesis in the mouse will be one of the major tasks of the scientific community and will require a dramatic change in the way of phenotyping and archiving of mouse models. INFRAFRONTIER will organise two complementary and linked European infrastructure networks for large scale and comprehensive phenotyping (Phenomefrontier) and archiving (Archivefrontier) of mouse models. INFRAFRONTIER will be embedded in a global effort to standardise and optimise the phenotypic characterisation of medically relevant models and in addition state of the art archiving and dissemination of such. Thus, INFRAFRONTIER will provide the umbrella of a pan-European effort to standardise and optimise the phenotypic characterisation of medically relevant mouse models and a state of the art archiving and dissemination of such important biological samples.

### 3. Scientific Case

There is consistent evidence for the conservation of molecular and cellular mechanisms between mouse and man. Furthermore, the availability and continuous development of unique classical, together with reverse genetics technologies applied in mice have provided to the scientific community the model of choice for the analysis of the human system in physiological and pathophysiological circumstances. INFRAFRONTIER, which consists of Phenomefrontier and Archivefrontier, will be the European platform to make best use of mouse models for the understanding of molecular and cellular networks underlying human health and disease. INFRAFRONTIER will enable European laboratories to make effective use of such mammalian models in the global effort to understand the logic of construction and functioning of complex systems.

**Phenomefrontier.** It can be envisioned that within the next decade over 25000 new mouse models will be generated in Europe. It will be necessary that this large number gets access to comprehensive functional and molecular characterisation. Phenomefrontier will provide a European platform, which will give access to comprehensive phenotyping to every laboratory including latest *in vivo* imaging technology and informatics tools to handle the phenotype data. Phenomefrontier is a programme that aims to play a leading role on the worldwide level.

**Archivefrontier.** To make full use of mouse models it will be essential to make them accessible to every laboratory in Europe. Archiving and distribution of mouse models under highest quality standards and dissemination of knowledge are the main topics of Archivefrontier. Instruments will have to be implemented which are not available currently. New freezing methods are being tested to optimise and speed up the process. The community will have to be trained to work with such material. The proposed infrastructure aims to play a leading role on the worldwide level. Mouse centres where research and infrastructure coexist, and that are leaders with respect to excellence and national importance, will be selected to become part of this infrastructure. The European Mouse Mutant Archive (EMMA) the infrastructure network which includes the most experienced European research institutions in the field will coordinate this project.

#### **4. Concept Case**

The main goal of functional genomics and mouse genetics in the 21<sup>st</sup> century will be the generation of mouse mutations for every gene in the mouse genome, creating a huge and vital resource of models for the study of human disease. Over the next decade, we can expect that tens of thousands of mouse disease models will become available, all of which will ultimately require archiving, dissemination and phenotyping.

Current capacity to achieve this goal is limited. Indeed, existing facilities across Europe can offer capacity for the dissemination and analysis of around a few hundred disease models per year. It will thus be necessary to organise phenotyping, archiving, and distribution of mouse models on a well-concerted, large-scale, pan-European level. INFRAFRONTIER brings together well-experienced European laboratories with proven track records to implement and run large-scale infrastructures. For the Phenomefrontier subproject two visibility studies have been undertaken.

1. Eumorphia performed the development of standardised and validated phenotyping assays in a wide variety of indications. 2. Eumodic, which is in the starting phase, will for the first time undertake large-scale phenotyping in a cross-laboratory effort. Both projects show clearly the well-organised scientific community and provide a structure, which will be developed for Phenomefrontier. Archivefrontier will be coordinated and run by EMMA. Archivefrontier is necessary to restructure the existing infrastructure. New members will be added and existing partners will have to undergo major upgrades to fulfil the upcoming demands of the scientific community.

EMMA was able to show great success in archiving and distribution of mouse models over the last years. This experience will increase the chances of success. Criteria have been developed to choose the essential and necessary partners for INFRAFRONTIER. The selection process includes national scientific organisations, national bodies and independent scientific advisory boards. The establishment of such an infrastructure will result in mutant mice becoming much cheaper, with an estimated decrease of the cost per strain by a factor of 5 to 10, while archived mice will not come with a series of restrictions, with a commercial supplier retaining the IP rights. NIH is planning such a bank of mutant mice and therefore Europe needs to keep pace and establish a similar infrastructure to be competitive.

#### **5. Further information, including strategic importance to ERA**

INFRAFRONTIER is necessary to ensure the appropriate coverage of phenotyping and archiving infrastructure in the different areas of Europe. INFRAFRONTIER is expected to give Europe a leading position in a worldwide competition on resources and knowledge for medically relevant mouse models. Europe will need such an infrastructure to make efficient use of emerging resources.

#### **6. Identification of other socio-economic impacts**

The launch of INFRAFRONTIER is required to speed up the discovery of molecular mechanisms of diseases and health - this is an important step for the future of molecular medicine and the advancement of diagnosis and therapy. Academia and industry will have to work together to develop new instruments and technologies for *in vivo* imaging using non-invasive methods. INFRAFRONTIER will not only be responsible for this task within Europe, it will take a global lead and will play an important part to ensure the appropriate advancement in science and the future of molecular medicine.

## 7. Participating Members

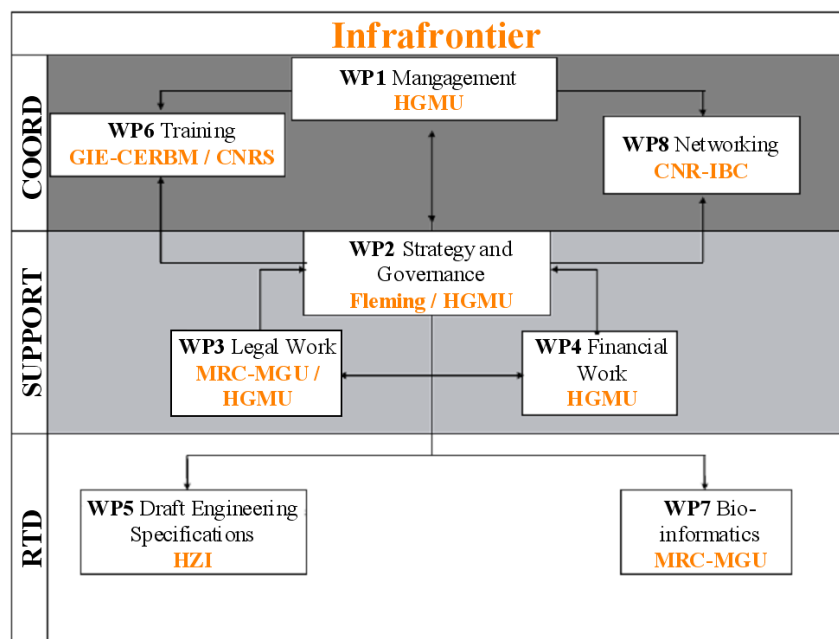
Scientific Partners	Funding Organisations (ministries, research councils)	Associated Partners
<ul style="list-style-type: none"> <li>- Helmholtz Zentrum München - German Research Centre for Environmental Health GmbH</li> <li>- MRC Mammalian Genetics Unit</li> <li>- Consiglio Nazionale delle Ricerche</li> <li>- Istituto di Biologia Cellulare</li> <li>- Centre Européen de Recherche en Biologie et en Médecine GIE – ICS</li> <li>- Genome Research Limited / Sanger Institute</li> <li>- Biomedical Sciences Research Centre Alexander Fleming</li> <li>- Karolinska Institute</li> <li>- Fundação Calouste Gulbenkian</li> <li>- Instituto Gulbenkian de Ciência</li> <li>- CNRS-CDTA</li> <li>- Universitat Autònoma de Barcelona</li> <li>- Consejo Superior de Investigaciones Científicas (CSIC)</li> <li>- University of Oulu</li> <li>- European Molecular Biology Laboratory</li> <li>- Helmholtz Centre for Infection Research GmbH</li> <li>- University of Copenhagen – Transgenic Core Facility</li> <li>- Czech Centre for Phenogenomics (BIOCEV z.s.p.o)</li> <li>- Veterinärmedizinische Universität Wien (Biomodels Austria)</li> <li>- Toronto Centre for Phenogenomics</li> </ul>	<ul style="list-style-type: none"> <li>- MRC (UK)</li> <li>- CNR (FR)</li> <li>- CERBM-GIE (FR)</li> <li>- Fundação Calouste Gulbenkian (IT)</li> <li>- CNRS (FR)</li> <li>- Hellenic Republic Ministry of Development (GR)</li> <li>- Helmholtz Association (DE)</li> <li>- German Ministry for Research and Education (DE)</li> <li>- Swedish Research Council (SE)</li> <li>- Generalitat de Catalunya, Departament de Salut (ES)</li> <li>- Parque Científico de Madrid (ES)</li> <li>- Comunidad de Madrid (ES)</li> <li>- Ministry of Education, Youth and Sports of the Czech Republic (CZ)</li> <li>- Institut National de la Santé et de la Recherche Médicale (FR)</li> <li>- General Directorate for Health Research of the Italian Ministry of Labour, Health and Social Policies (IT)</li> </ul>	<p>Observer status:</p> <ul style="list-style-type: none"> <li>- Belgium</li> <li>- Norway</li> </ul>

## 8. Budgetary Information

Preparatory cost (total / EC contribut.)	Construction cost (total)	Operation cost (annual costs)	Re- and decommissioning cost (total in Mio €)
4,8 Mio € / 4.5 Mio €	180 Mio €  Construction of new facilities and major upgrades of the existing facilities	average of 80 Mio €  ~ 0.9 to 1.0 Mio € for the central coordination unit  Assigning new phenotypes to new	Not applicable

		mouse models from different pipelines. Archiving new mouse models including attached data sets within an upgraded database.	
<b>9. Timetable until operation</b>			
Preparatory phase 2008 – 2010	Construction phase 2010 - 2014	Operation 2010 onward	Re- and decommissioning
<b>10. Contact</b>			
<p>Prof. Dr. Martin Hrabé de Angelis Coordinator of INFRAFRONTIER Director of the Institute of Experimental Genetics email <a href="mailto:hrabe@helmholtz-muenchen.de">hrabe@helmholtz-muenchen.de</a></p> <p>Dr. Michael Raess Project Manager of INFRAFRONTIER email <a href="mailto:michael.raess@helmholtz-muenchen.de">michael.raess@helmholtz-muenchen.de</a></p> <p>Helmholtz Zentrum München German Research Center for Environmental Health (GmbH) Institute of Experimental Genetics Ingolstaedter Landstr. 1 D-85764 Neuherberg Germany</p> <p><a href="http://www.infracontier.eu">http://www.infracontier.eu</a> <a href="http://www.helmholtz-muenchen.de/en/ieg/">http://www.helmholtz-muenchen.de/en/ieg/</a></p>			
<b>11. Progress in the Preparatory Phase</b>			
<p><b>Overall strategy and general description:</b></p> <p>The INFRAFRONTIER Preparatory Phase is a project of three years duration commenced in March 2008. The work plan was broken down into eight work packages (see Figure 16). Of central importance are INFRAFRONTIER work package 2 (<b>Strategy and Governance</b>), work package 3 (<b>Legal work</b>) and work package 4 (<b>Financial work and funding</b>). WP2 defines the INFRAFRONTIER mission, its vision, the governance structure of the planned infrastructure in operation and the services of the new infrastructure. The overall strategy is defined by an iterative process involving WP2, WP3 and WP4 and will be summarised in a strategic plan for the implementation phase. WP3 determines the most suitable legal status of the planned infrastructure. Furthermore, drafting, negotiating and signing a Memorandum of Understanding (MoU) between all partners involved, will contribute to long-term stability of the consortium. WP4 works out a sustainable funding concept for the new infrastructure and provides a business plan for the construction phase.</p>			

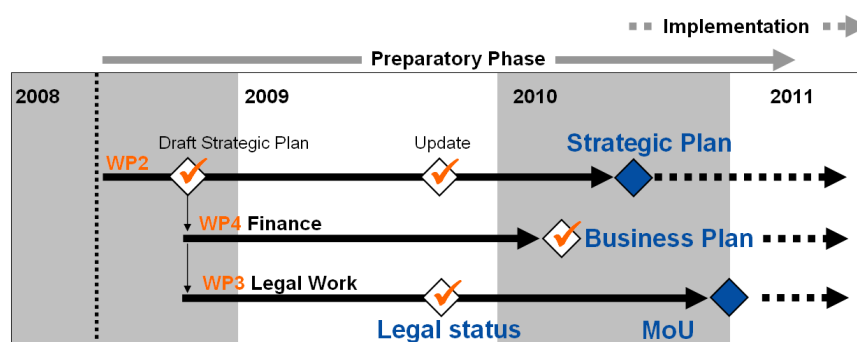




**Figure 16:** Work packages of INFRAFRONTIER

All partners are involved in WP2, WP3 and WP4. Related to their central importance these three work packages will provide the **key deliverables of INFRAFRONTIER** which are (see Figure 17):

- 1) The identification of the most suitable **legal status**
- 2) A **business plan** based on a sustainable funding concept
- 3) A **legal agreement** between all partners
- 4) A **strategic plan** for the construction phase



**Figure 17:** Key deliverables of WP2, WP3 and WP4 of INFRAFRONTIER

These support activities are complemented by two technical work packages. **WP5 (Draft engineering specifications)** supports the construction of new animal facilities. **WP7 (Bioinformatics)** assesses the IT systems of the existing mouse clinics and archiving centres and provide recommendations on the best mouse management and laboratory information management systems (LIMS) for the new partners. Furthermore, work is undertaken to facilitate and ease the exchange of data among the INFRAFRONTIER partners. **WP6 (Training)** ensures the transfer of know-how between partners aiming at the establishment of common standards among all scientific partners of the new infrastructure. **WP8 (Networking)** ensures the alignment of the planned services of the new infrastructure with the needs of the

European mouse functional genomics and biomedical research community. Potential new INFRAFRONTIER partners particularly from new EU Member States will be identified and the INFRAFRONTIER activities will be embedded in global efforts related to archiving and distribution and mouse phenome database integration. **WP1 (Management)** concerns the project management of INFRAFRONTIER.

#### **Progress towards the central objectives**

The INFRAFRONTIER members drafted a strategic plan in June 2008 that was updated on a strategy meeting in September 2009. The strategic plan provided the basis for the activities in the legal and financial work packages. The available options for a legal framework were thoroughly assessed; particularly the ERIC legal framework specifically developed for European Research Infrastructure initiatives. This assessment led in September 2009 to the recommendation of establishing an ERIC for the central coordination unit of INFRAFRONTIER. The monitoring of the development of alternative legal frameworks (e.g. the EMBL Special Project) is nevertheless ongoing. Legal frameworks and funding strategies of existing Research Infrastructures and the funding instruments of the European Investment Bank (EIB) were explored in a series of dedicated workshops that were organised together with the other ESFRI BMS Research Infrastructure initiatives. The financial requirements as well as funding commitments from national and international sources were reviewed and the development of a business plan was finalised in May 2010. The business plan and draft statutes for the INFRAFRONTIER legal entity were discussed with all stakeholders in June 2010. INFRAFRONTIER work packages 2, 3, 4 and an Inter-Ministry working group will use these documents to detail the final strategic plan and a Memorandum of Understanding for the implementation phase. With the approval of these central milestones of the Preparatory Phase by the partners the implementation of the pan-European INFRAFRONTIER Research Infrastructure can be initiated.

#### **RTD and coordination activities**

In a series of site visits generic engineering specifications for phenotyping and archiving facilities were created. A detailed report was finalised in early 2010; a shorter summary for publication is being prepared. Based on surveys on existing data and workflow management systems in mouse cryo-repositories and phenotyping facilities detailed recommendations are being developed. In a series of dedicated training courses state of the art know-how of cryo-preservation and systemic phenotyping was disseminated within the consortium. The activities of INFRAFRONTIER were publicised in media targeted at researchers and policy makers, on the project web site ([www.infrafrontier.eu](http://www.infrafrontier.eu)), by providing information material and by presenting INFRAFRONTIER at scientific events and conferences. A specific survey was undertaken to identify potential members in the new EU Member States. This survey forms the basis of INFRAFRONTIER's networking activities in these countries. INFRAFRONTIER participates in a global user survey on phenotyping requirements and has undertaken a benchmarking of global phenotyping and archiving activities (see Figures 18 and 19).

#### **Central management**

The INFRAFRONTIER coordination regularly interacted with the European Commission, ESFRI, the ESFRI BMS Thematic Working Group, national and European policy makers, national funding institutions and the scientific community. INFRAFRONTIER together with the other BMS initiatives collaborates in the EMTRAIN initiative with representatives of the European pharmaceutical industry to establish a European medicines research training network. The BMS initiatives also started a process to establish their common requirements for a data infrastructure.

In December 2009 scientific and administrative partners from the **Czech Republic, Austria** and **Canada** became full members of the INFRAFRONTIER consortium. This documents the significance of the new EU Member States for achieving the objectives of INFRAFRONTIER as well as the global dimension of the project.

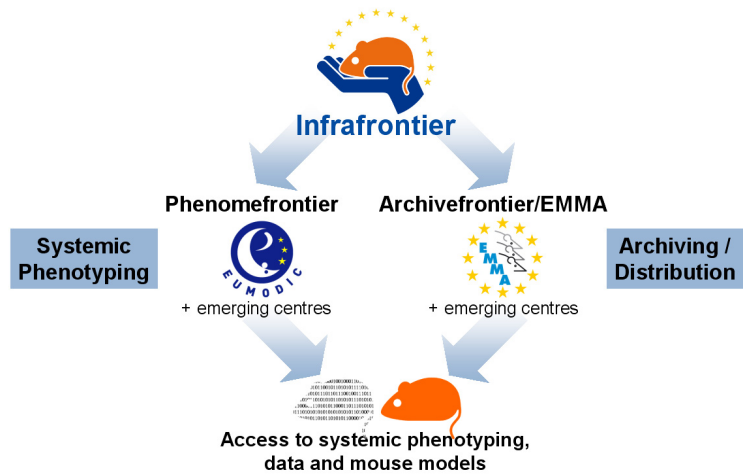


Figure 18: Overview about INFRAFRONTIER's deliverables

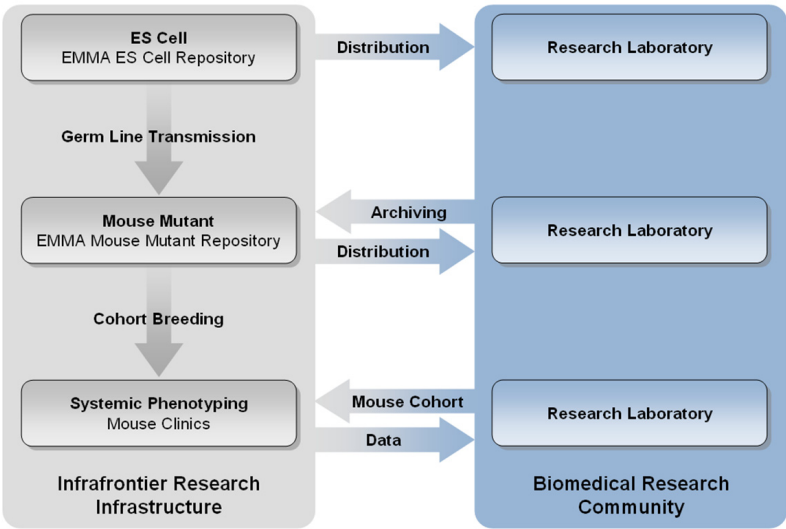






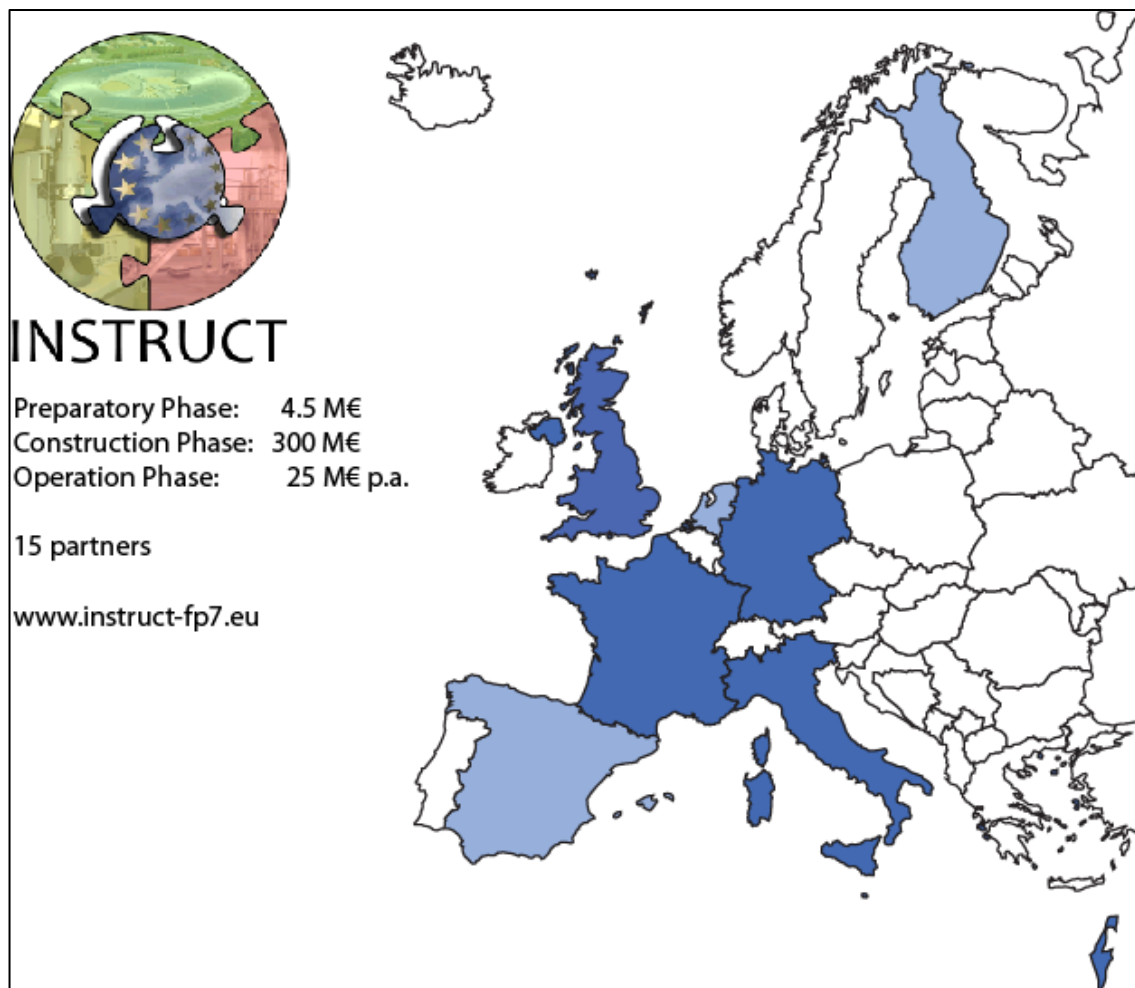


Figure 19: INFRAFRONTIER's networking activities with the biomedical research community

**Table 9:** Links between Research Infrastructures - INFRAFRONTIER

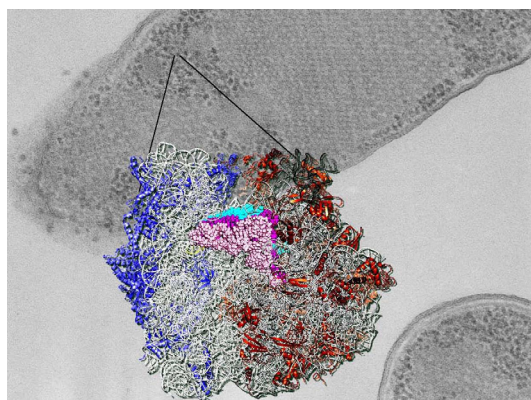
	Infrafrontier	Further specification of the technological link	Further specification of the thematical link	Short statement for further specification (last update July 2010)
BBMRI		Biobanking of biological samples of mouse models of human diseases; Disease Phenotype Characterisation	Mapping of mouse and human phenotypic descriptions and disease ontologies	Infrafrontier's biobanking activities of mouse tissues will draw on BBMRI's expertise on biobanking of human material. Mapping of disease ontologies and phenotype descriptions in man and mouse will create enormous added value
EATRIS		Provision of disease-specific mouse models for efficacy tests and mouse models for safety evaluations.	Preclinical testing of novel medicinal products developed in EATRIS in suitable mouse models of INFRAFRONTIER.	EATRIS and Infrafrontier will collaborate on preclinical testing of novel drugs and treatments in mouse models for human diseases
ECRIN		Development of animal models and phenotyping techniques in line with the clinical symptoms and biomarkers used in clinical research	Development of pan-European strategy and shared tools for education and training programme (IMI/ www. emtrain.eu)	
ELIXIR		e-Infrastructure for comprehensive sets of genomics data and phenotype data	Support data infrastructure, data interoperability and standardisation of mouse model related data	ELIXIR provides e-infrastructure for systemic phenotyping, archiving and distribution of mouse models of human diseases
INSTRUCT		<i>In vivo</i> assays of bioactive compounds Functional data to relate to molecular structure and vice versa	Structure/function of proteins for biomedical research	These infrastructures link together to allow investigation of systems spanning from molecule to organism.
EMBRC		Extension of 'omics' technologies to marine organisms; <i>in vivo</i> testing of marine compounds in mouse clinics	Mapping of genotypic and phenotypic information	
ERINHA				
Euro-BioImaging		Access to cutting-edge small animal imaging devices	Imaging studies for diseases mechanisms and new therapeutic approaches in animals	Collaboration on imaging methods for mouse models, e.g. by establishing common imaging programs, common imaging technology development for small animals
EU-Openscreen		Bioactive compounds and drug leads for <i>in vivo</i> testing; <i>in vivo</i> mode of action	Proof of concept for <i>in vivo</i> activities of biologically active compounds	Bioassays of compounds from EU-Openscreen test pipelines in Infrafrontier mouse clinics
e-IRG		Explore remote image data storage and processing		Euro-BioImaging and Infrafrontier plan together with EUDAT a pilot project to define requirements and explore solutions for an image warehouse that provides fast and distributed access and includes tools for navigation, visualisation, and annotation of image data.
SSH				
ESP				
ENV				
ENE				

#### 4.5.6 Integrated Structural Biology Infrastructure (INSTRUCT)



Structural biology in the next two decades aims to integrate structural knowledge at different resolution levels into specific cellular contexts, with a temporal component, to underpin biomedical issues. This challenge requires the seamless integration of manifold techniques providing maximum information in different

resolution ranges. INSTRUCT will link the information obtained by the major structural biology methods with state of the art cell biology techniques to provide a dynamic picture of key cellular processes at all scales (see Figure 20).



**Figure 20:** Virus particle arrays are shown by electron microscopy in a bacterial cell section, along with ribosomes for which an expanded structural representation is shown. (EM courtesy of Dennis Bamford, University of Helsinki; ribosome structure courtesy of Venki Ramakrishnan, LMB Cambridge)

Major technology advances, from high throughput methods in protein production, through NMR and X-ray crystallography to electron microscopy mean that major investment in infrastructure is required to maintain European competitiveness and develop the newer technologies at the interface with cell biology (cryo-electron tomography, correlative microscopy, X-ray imaging, single molecule techniques and in-cell NMR). The Preparatory Phase of INSTRUCT started the 1<sup>st</sup> of April 2008.

Following recommendations from the working groups (<http://www.instruct-fp7.eu>), the operational structure of INSTRUCT has been established, anchored by 7 core centres offering a broad range of high-level technologies for structure determination integrating molecules to cellular resolution levels: Division of Structural Biology, University of Oxford, UK; IGBMC-CERBM, Illkirch, France; CIRMMP-CERM, Florence, Italy; Max-Planck-Institute of Biochemistry, Martinsried, Germany; Max-Planck-Institute of Biophysics, Frankfurt, Germany; Weizmann Institute of Science, Rehovot, Israel; EMBL sites at Hamburg, Grenoble, Heidelberg, France and Germany. Seven associate centres have also been established following a call for proposals and an independent review. These provide

specialist or complementary expertise to the core centres: Associate Centre in Mass Spectrometry for Native Proteins and Complexes (University of Utrecht and University of Oxford, The Netherlands and UK); Associate Centre in Integrated Structural Bioinformatics (Tel Aviv University, Israel); Associate Centre for Large Scale Virus Production (University of Helsinki, Finland); Associate Centre for Software in Image Processing (CSIC-Madrid, Spain); Associate Centre for Mammalian Cell Expression (Helmholtz Centre for Infection Research-Braunschweig, Germany); Associate Centre for Solid State NMR (Leibniz-Institut für Molekulare Pharmakologie-Berlin, Germany); Associate Centre for Computational Structural Biology (Rutherford Appleton Laboratory, UK). An open call for national affiliate centres, themselves centres of excellence within the context of their host country, will provide access to, and expertise in, key structural biology technologies for national, and in most cases trans-national, users and will play a key role for some member countries or regions in developing their structural biology infrastructure provision and connecting with European networks.

After lengthy consideration, the legal model chosen for INSTRUCT for the first operational period is a combination of a Memorandum Of Understanding defining the project and the agreement between its members and setting out their rights and responsibilities, and a Special Purpose Vehicle (SPV) – a UK-based company limited by guarantee (a not for profit company) that will be the “doing” vehicle for INSTRUCT as a legal entity that can enter into contracts on behalf of INSTRUCT, for example to employ staff. This will be implemented through a central INSTRUCT office, located initially in Oxford, UK.

The governance and management of INSTRUCT will be carried out through the INSTRUCT council, executive committee, board of directors for the SPV, centre committee, operations committee and the independent science advisory board.



### 1. Name and descriptive title

## INSTRUCT - Integrated Structural Biology Infrastructure

### 2. Short description of new RI or major upgrade and main characteristics

The new infrastructure is expected to consist of seven distributed core centres for integrated structural biology, each with a broad complement of core technologies and linked biological foci to drive the development of infrastructure expertise. All centres will maintain and further develop a set of core technologies such as protein production, NMR, crystallography, and different forms of microscopy. Each centre will shape their infrastructure development plan from the scientific need to improve the production and analysis of functional complexes. Development of infrastructure in each core centre will include the identification and design of new-build infrastructure capabilities, upgrading of existing facilities to incorporate the newest technological capabilities and the maintenance of existing technologies in such a way as to provide access for the user community through the development and implementation phase of the project. The network of centres will be organised in order to obtain multi-scale structural data and translate these data into functional knowledge. In doing this, the specific aims of the project will be:

1. To define fully the appropriate composition of core and associate centres to provide an optimal European infrastructure.

Criteria:

- i) Scientific excellence, ii) Scientific coverage, iii) Strong record in technology & methods development, iv) Commitment to collaborative infrastructure, v) Biomedical engagement, vi) National commitment

2. To establish the correct balance of infrastructure provision required to permit existing and developing technologies to mesh effectively between the different levels of resolution in structural biology, from the molecular to the cellular and ultimately the whole organism scale, thus providing a dynamic picture of key biological processes.

Criteria:

- i) Likely interdisciplinary impact of technologies, ii) European leadership in each area

3. To establish a plan to enter rapidly the operations phase of INSTRUCT whilst running the construction phase activity alongside this.

Criteria:

- i) Key core technologies provided at the end of the Preparatory Phase, ii) Integrative technologies developed in parallel.

INSTRUCT aims to establish a balance of national and pan-European activity that will ensure that the major centres can be supported by national funding mechanisms whilst building a viable business plan that allows pan-European access.

### 3. Scientific Case

#### **The scientific challenge:**

The major challenge for structural biology in the next two decades will be the integration of structural knowledge at different resolution levels into specific cellular contexts. This will underpin biomedical sciences. This challenge requires the combination of techniques providing information in different resolution ranges - appropriate to each of the required scales - and bridging the gaps between them. Furthermore, besides this static picture of a cell, there is a temporal component that is crucial and understanding cell biology requires understanding the dynamics of the different cellular processes. Going beyond the single protein approaches to

identify, characterise and analyse the individual structural assemblies and subassemblies of a cell, it is now important to integrate the information obtained by the major techniques (NMR, X-ray and electron crystallography, electron and light microscopy) and develop the necessary mathematical methodology to combine the resulting information. In addition, integration with state-of-the art cell biology techniques (of which light microscopy of living cells is already an important part) is another essential aspect, providing a dynamic picture of many of the key processes (intra-cellular trafficking, for instance) at all scales.

**Establishing infrastructure to meet the challenge:**

One impact of the major technology advances, from parallel methods for protein production, though NMR and X-ray crystallography to electron microscopy and tomography is that substantial investment in infrastructure is now required to maintain European competitiveness in this core aspect of biology. The development of the INSTRUMENT infrastructure is driven by fundamental biological questions linked to human health (cancer, infectious diseases, host-pathogen interactions, etc.) and/or environment problems (adaptation of life to extreme conditions: temperature, heavy metals, radiation, toxic molecules). These infrastructures will provide world-class facilities and maintain Europe's competitiveness in structural biology. The requirements for highest precision instrumentation will challenge European industry to improve their capabilities and the use of the facilities for industrial research will strengthen Europe's industrial competitiveness in particular in bio-pharma companies (INSTRUMENT will engage directly with these companies) and areas such as electron optics. Key technical bottlenecks will be addressed jointly with appropriate European SMEs. The project will include an interdisciplinary training programme in biology, chemistry and physics relevant to the expertise needed in structural biology.

Each core centre will develop its own scientific programme and continue to develop technological and methodological cutting edge expertises in various approaches. The centres will be complementary to one another. In addition to the cores, technology will be made available from associate centres, where smaller, more focused technologies will be developed for access. Both cores and associates will deliver a significant fraction of their activity via open-access for the user community. Access will be facilitated by a network of affiliate centres who represents the interests of national stakeholders, both to the local funding bodies and, in INSTRUMENT, to help establish strategic priorities.

#### 4. Concept Case

Structural biology has an illustrious history in Europe. We are now at a turning point in the impact of structural studies on biology, as sample production technologies mature and key core techniques become increasingly powerful, but escalate in cost. The challenge is to maintain the momentum built up, especially by the coordinating actions of EC funding in FP5 and 6, to establish the core centres, associated centres and national coordinators who can provide and effectively use a robust infrastructure to take the integration of methods to the next level, keeping Europe competitive as structural biology evolves into integrative structural cell biology. The INSTRUMENT proposal represents the next step: to make concrete preparations to implement the infrastructure.

A major objective of the preliminary phase has been to establish the optimal *modus operandi* for INSTRUMENT. The partnership brings together a very strong scientific collective body with European and global eminence in the area of structural biology to orchestrate the operation of a large integrated initiative at all levels of science, technology and governance. The centres will be networked to a wider community to capture multi-scale data and translate these into functional knowledge.



**5. Further information, including strategic importance to ERA*****Scientific strength of Europe in structural biology:***

The research community in structural biology within the ERA is extensive and well-established. The community spans seamlessly from both fundamental and translational academic research through to the numerous Europe-based biotech and pharma companies and drives a huge diversity of commercial development of methodologies and instrumentation. INSTRUMENT draws on the vibrancy of the interface between structure biology research and commercial development by the inclusion of a European company as a Partner and by the involvement of a cohort of companies (the majority SMEs) in feasibility studies that have informed the infrastructure development plan. European laboratories have consistently played a pioneering role throughout the development of structural biology (as testified by the number of European Nobel prize winners in this field). The research community has a unique history of inter-laboratory pooling of developments to drive forward cutting edge research (for example the efficient pooling of crystallographic software via Collaborative Computational Project Number 4, CCP4) most recently supported and promoted at a pan-European level by EC funding (as discussed in the following section) and in terms of large scale facilities exemplified in the development and use of intense X-ray and neutron sources. For such sources structural biology research has already necessitated levels of capital investment beyond the normal means of a single research institution and in many cases requires the international cooperation of several countries for the largest facilities. European structural biology has benefited from a very large effort based around synchrotron facilities (European Synchrotron Radiation Facility (ESRF), Deutsches Elektronen-Synchrotron (DESY), Positron-Elektron-Tandem-Ring-Anlage (PETRA), Berliner Elektronenspeicherring-Gesellschaft für Synchrotronstrahlung (BESSY), Swiss Light Source (SLS), Ligne Utilisée pour la Caractérisation par Imagerie et Absorption (LUCIA), Centre de rayonnement synchrotron français (SOLEIL), Dipole And Multipole Output for the Nation at Daresbury (DIAMOND), ELETTRA Synchrotron Light Laboratory and MAX-lab) and neutron sources (ILL, Jülich and ISIS). INSTRUMENT will build on these foundations to tackle the diverse and evolving challenges of providing an infrastructure for the transition from molecular to cellular structural biology.

***Potential for INSTRUMENT to add value:***

- a. INSTRUMENT will provide a well-coordinated pan-European effort to provide the capacities and expertise needed to contribute to the continued development of existing technologies and the implementation of emerging technologies in structural biology. INSTRUMENT will develop infrastructures to a greater level of integration than has so far been possible in European structural biology by tying in several existing national initiatives into the European framework.
- b. INSTRUMENT will integrate core centres combining excellence in all major areas of structural biology with associate centres providing further technical expertise and access to infrastructure. Flexibility in the composition of participants is inherent in the project structure: a key objective of the Preparatory Phase is to evaluate groups for their ability to provide access to technology and specific expertise at each level and provide a mechanism to include new participants at all levels of core centre, associate centre or user.
- c. INSTRUMENT will also benefit from forming links with other BMS initiatives. European structural biology has maintained strong links with EMBL-EBI over many years, most recently through the Structural Proteomics in Europe (SPINE), e-science resource for high-throughput protein crystallography (eHTPX) and Protein Information Management System (PIMS) projects and will continue to build on this excellent relationship through ELIXIR to develop resource and data handling in parallel to the hardware technologies being developed by INSTRUMENT. Links with the other BMS initiatives are now also well-defined.

## 6. Identification of other socio-economic impacts

The structural biology community has a very strong track record for using EC input as a catalyst for national investment and for genuine scientific coordination. This was demonstrated by the effects of the FP5 IP SPINE, which galvanised a number of laboratories across Europe, at a time when Europe was falling dangerously behind in terms of infrastructure and technology development for high-throughput structural proteomics. The remarkable speed of uptake of technologies demonstrated as effective in the SPINE context (for instance small-volume crystallisation methodologies) allowed Europe to catch up and remain competitive. Since SPINE there have been a significant number of other projects, covering most areas of structural biology, which have maintained a strong culture of development and exchange, which allows Europe, in many cases, to punch above its weight, in terms of scientific output. In addition EC funding via Integrated Infrastructure Initiative (I3) grants has provided a very effective mechanism for facilitating access to infrastructure.

INSTRUCT will continue this mission in providing cutting edge technologies, training young scientists and identifying new goals for structural biology development in the future. It will encourage European scientists to find solutions to previously difficult cross-border infrastructure sharing arrangements and to benefit from the exchange of knowledge, co-development opportunities and the possibility of cost recovery for the technologies.

The pressing need for more advanced structural cell biology data is illustrated in the 2008 World Health Report, which ranked infectious diseases as the third of the top five causes of death in low income areas. To develop new treatment and prevention strategies, a better understanding of the structure and function of individual pathogens is essential. INSTRUCT will allow a faster, more coordinated response to new threats such as pandemics or bioterrorism and will contribute to the design of innovative, effective and safe vaccines, holding out the possibility of the global elimination of certain human and animal diseases. Any reduction in the burden of disease through improved prevention and/or treatment produces considerable potential economic gains, as well as contributing to healthier ageing and improved public health.

## 7. Participating Members

Scientific Partners	Funding Organisations (ministries, research councils)	Associate Centres
<p>P1. University of Oxford, UK</p> <p>P2. CERBM, Strasbourg, France</p> <p>P3. EMBL (Grenoble, Hamburg, Heidelberg sites)</p> <p>P4. CIRMMP, Florence, Italy</p> <p>P5. Weizmann Institute, Israel</p> <p>P10. Max-Planck-Society (Munich and Frankfurt sites), Germany</p> <p>P12. Bruker Biospin GmbH, Germany</p> <p>P14. University of York, UK</p>	<p>P6. Medical Research Council (UK)</p> <p>P7. CNRS (FR)</p> <p>P9. MOST (IS)</p> <p>P11. BMBF (DE)</p> <p>P13. CNR (IT)</p> <p>P15. CEA (FR)</p>	<p>a. Associate Centre in Mass Spectrometry for Native Proteins and Complexes (University of Utrecht and University of Oxford, The Netherlands and UK))</p> <p>b. Associate Centre in Integrated Structural Bioinformatics (Tel Aviv University, Israel)</p> <p>c. Associate Centre for Large Scale Virus Production (University of Helsinki, Finland)</p> <p>d. Associate Centre for Software in Image Processing (CSIC-Madrid, Spain)</p> <p>e. Associate Centre for Mammalian Cell Expression (Helmholtz Centre for Infection Research-Braunschweig, Germany)</p>

		f. Associate Centre for Solid State NMR (Leibniz-Institut für Molekulare Pharmakologie-Berlin, Germany) g. Associate Centre for Computational Structural Biology (Rutherford Appleton Laboratory, UK)	
8. Budgetary Information			
Preparatory cost (total in Mio €):  4.5 Mio €	Construction cost (total in Mio €)  300 Mio €	Operation cost (total in Mio €):  25 Mio €/year (includes underwritten infrastructure and access costs) Coordination office: running costs estimated at 750K €/year	Re- and decommissioning cost (total in Mio €)  50 Mio €
9. Timetable until operation			
Preparatory phase  2008-2011	Construction phase  2011-2018	Operation  2012-2018	Re- and Decommissioning  2012-2017
10. Contact			
Professor David I Stuart, Division of Structural Biology, University of Oxford, UK <a href="http://www.strubi.ox.ac.uk">http://www.strubi.ox.ac.uk</a>			
11. Progress in the Preparatory Phase			
<p><b>Sign-up by European Member States:</b> Twenty two European Member States have provided formal expression of interest in joining INSTRUCT and will be considering the funding proposal during 2010. The INSTRUCT council, comprising a membership made up of Member States (which may often be represented by funders), will oversee the strategic and scientific development of INSTRUCT. The milestones and timetable for the implementation of INSTRUCT are shown in Table 10.</p> <p><b>Organisation of INSTRUCT:</b> The organisational structure of INSTRUCT comprises a dynamic distributed infrastructure of complementary core, associate and national affiliated centres of excellence open to external user access and driving technical innovation (see Figure 21). These are defined as:</p> <p><b>a. Core Centres</b> providing trans-European access to ~20% of total activity for a range of state of the art structural biology technologies and integrative biological approaches and expertise, often offering access to a “pipeline” of related technologies;</p> <p><b>b. Associate Centres</b> offering specialised technologies or services complementary to those provided by core centres and essential to the development of integrative structural biology, for example specialist sample production, mass spectrometry, software development; and</p>			

**c. National Affiliated Centres** are centres of excellence that provide additional opportunities for access to specific structural biology technologies. An open call for national affiliate centres will be published in August 2010.

**Draft criteria for National Affiliated Centres** - INSTRUMENT national affiliated centres will:

- Be a centre of excellence within the context of their host country
- Provide some, not necessarily all, of the core INSTRUMENT technologies
- Show evidence of an intention to move towards integrated structural biology approaches
- Offer access to national affiliated centre facilities to national, and possibly non-national, users
- Be capable of, and willing to organise training programmes in collaboration with INSTRUMENT
- Be willing to participate in the transfer of relevant new technologies to/from INSTRUMENT

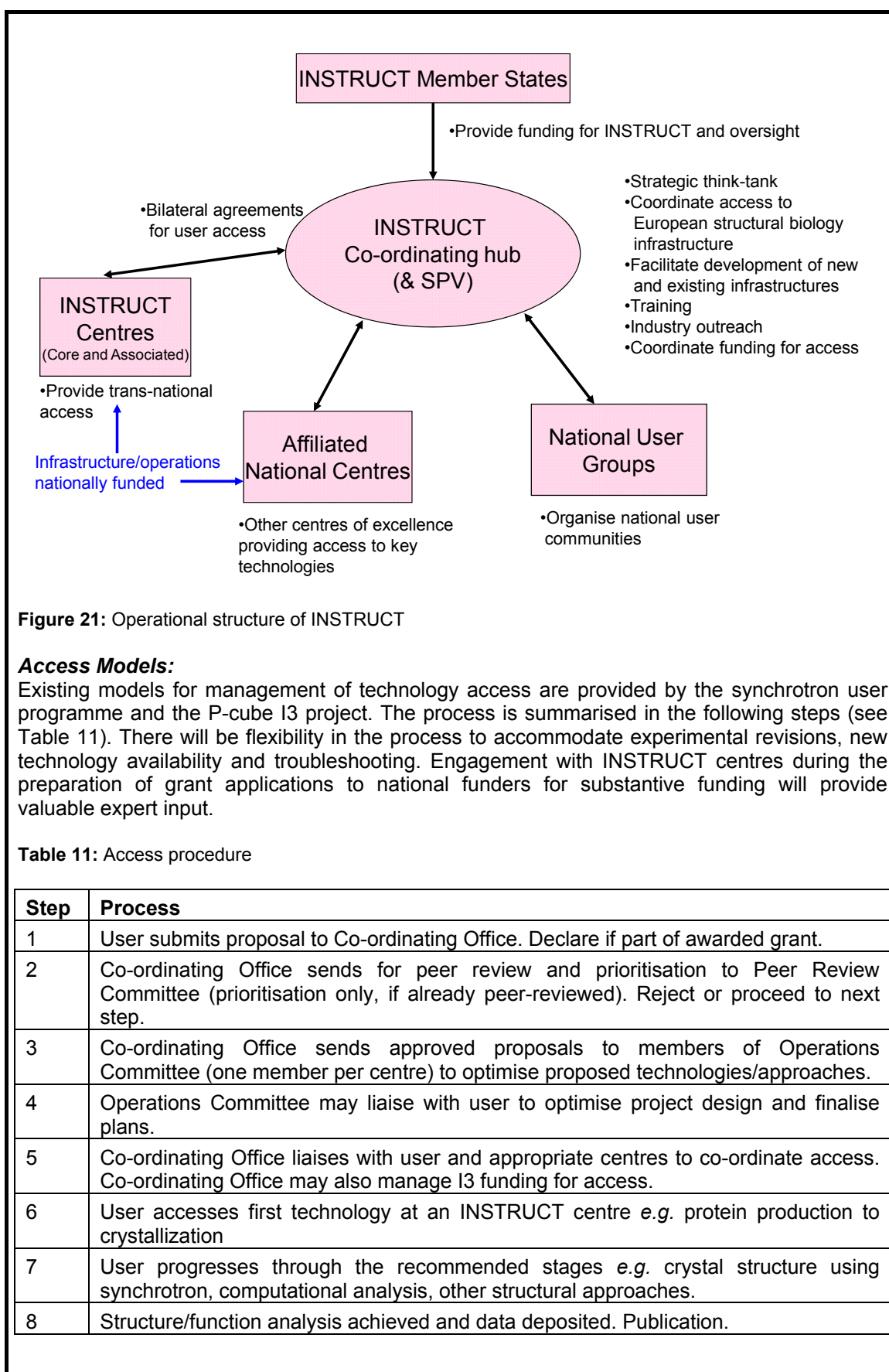
**d. National User Groups** will coordinate the development of national “roadmaps” for structural biology, identifying national gaps in technology provision and scientific and technical opportunities that INSTRUMENT can help to address, and contributing to the development of INSTRUMENT strategy. National user groups may, in many cases, be managed by national affiliated centres. National user groups will provide a forum through which scientific and technical interactions between national groups and other INSTRUMENT Member States can be enabled, whether or not they have an INSTRUMENT centre.

**e. A central INSTRUMENT “hub”** will be established to run INSTRUMENT, coordinating the provision of access to core and associate centres and funding for trans-national access, facilitating access to national affiliated centres, and managing outreach to stakeholders including industry, the provision of training and calls for proposals for R&D. Initially, the hub will be sited in Oxford alongside the Oxford core centre.

**Table 10:** Milestones and timetable for the implementation of INSTRUMENT

Milestone	J10	A10	S10	O10	N10	D10	J11	F11	M11	A11	M11	J11
Funding proposal drafted	●											
MOU agreed	●											
Company papers drafted			●									
IP policy drafted			●									
Communications strategy drafted			●									
Access peer review established			●									
BioNMR operations start				●								
BIOSTRUCT submitted					●							
Funding proposal decision						●						
Company papers agreed						●						
Early commitment from ≥2 member states achieved						●						
IP policy accepted						●						
Committees established						●						
Website set up							●					
Access process agreed							●					
Training programme drafted							●					
Training programme approved								●				
Staff appointed									●			
Hub operational										●		
BIOSTRUCT funding decision											●	
1st users												●

\*BIOSTRUCT is the synchrotron I3 proposal.

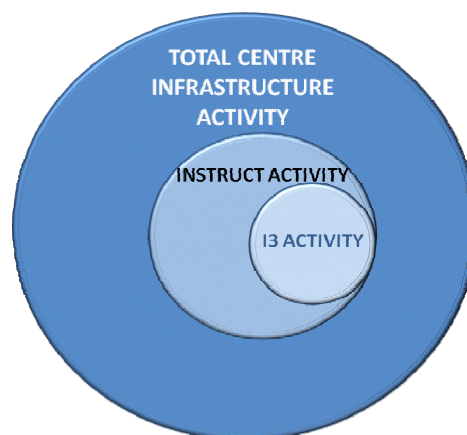


***The operational scope of INSTRUCT:***

Each centre will offer infrastructure for access. The majority of this (approximately 80%) will continue, as currently, to be for users of their choice funded from grants, institutions, national funds etc. INSTRUCT will not manage this access. Centres will also continue with their own R&D and training programmes

INSTRUCT activity: Around 20% of access will be made available for INSTRUCT activity. Centres may also be involved in INSTRUCT R&D (pilot studies) and training programmes. Access and R&D will be subject to INSTRUCT rules – i.e. for Member States, subject to peer review, and will be part or wholly funded from any of the following sources: I3, industrial sponsorship, subscription fees. The access and R&D programmes will include advice on an integrated approach that may involve other INSTRUCT centres and technologies, new technology platforms and access to development projects. INSTRUCT will manage this access.

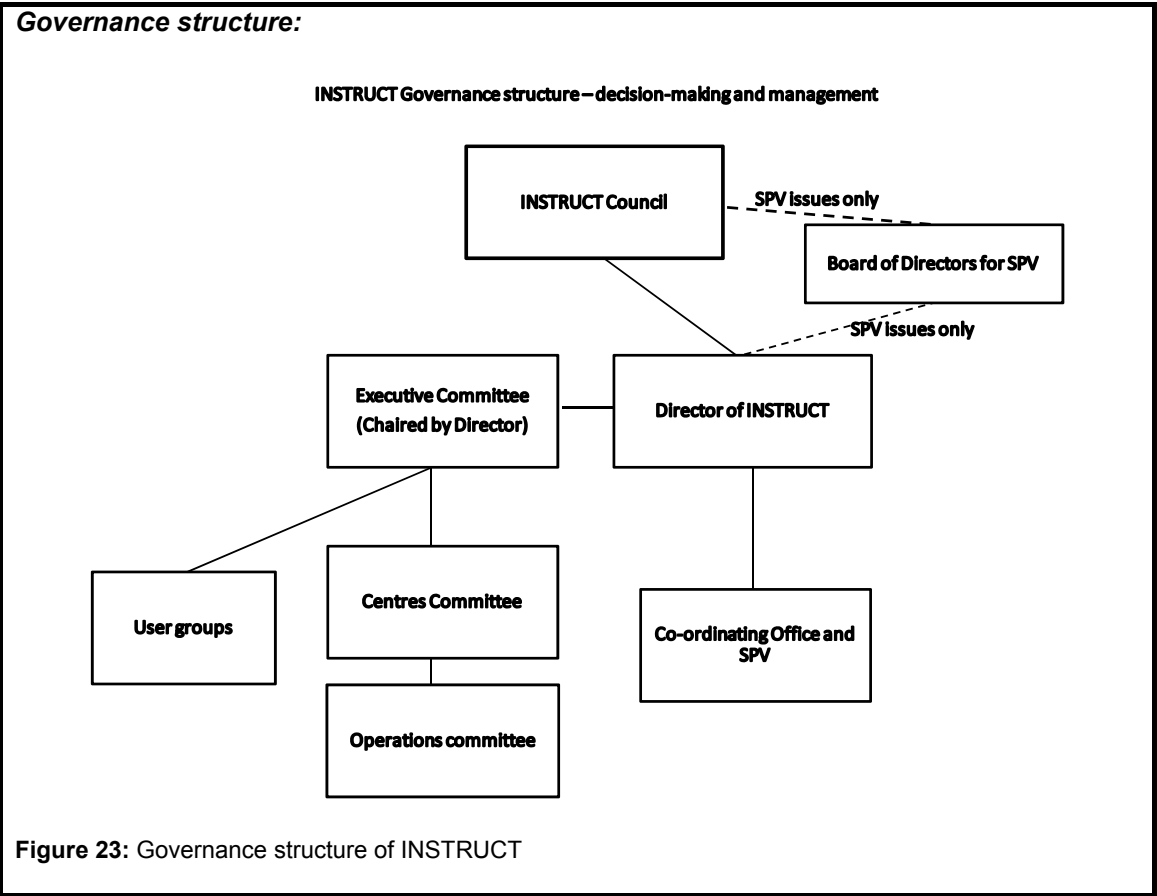
Within the total INSTRUCT activity, a proportion (at present undefined) will be available (subject to EC rules) for open access through the I3 programme. INSTRUCT will manage this access, as future I3s in this area will be coordinated by INSTRUCT (see Figure 22).



**Figure 22:** Operational scope of INSTRUCT

***Legal model:***

After considering a variety of models the legal model chosen for INSTRUCT is a combination of a Memorandum Of Understanding defining the project and the agreement between its members and setting out their rights and responsibilities, and a Special Purpose Vehicle (SPV) – a UK-based company limited by guarantee (a not for profit company) that will be the “doing” vehicle for INSTRUCT as a legal entity that can enter into contracts on behalf of INSTRUCT, for example to employ staff. All of the strategic and scientific direction for the INSTRUCT project will be provided through the INSTRUCT Council (the signatories to the MOU). The governance model is given below (see Figure 23). This arrangement will be reviewed by the council after an initial period of operation to assess if the needs of INSTRUCT would be better met by a structure based around the EC ERIC vehicle.



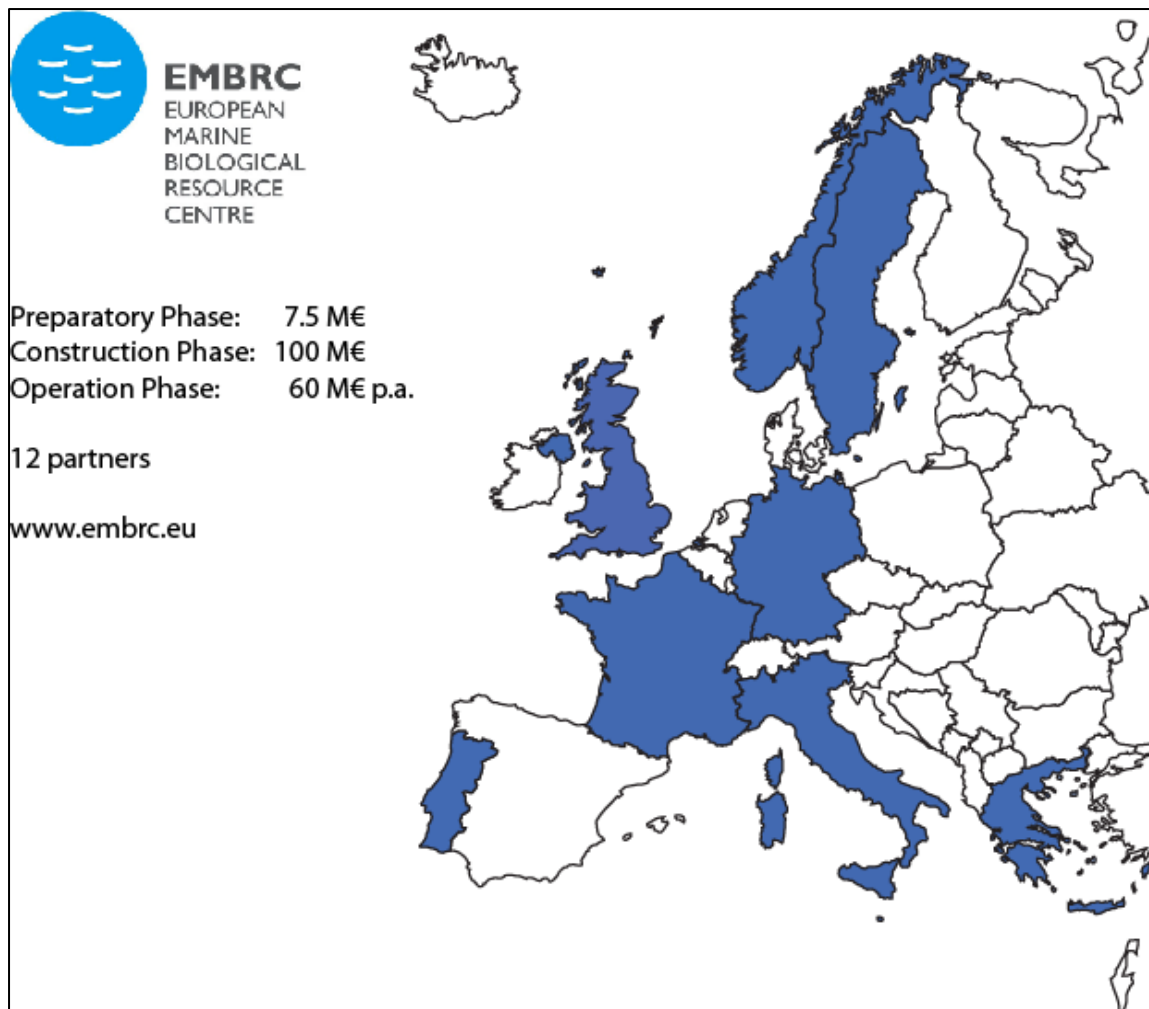
**Table 12:** Links between Research Infrastructures - INSTRUCT

	INSTRUCT	Further specification of the technological link	Further specification of the thematic link	Short statement for further specification (last update February 2010)
BBMRI		Biomedical data to relate to molecular structure	Biomedical research	INSTRUCT has been working together with all the BMS preparatory phase projects in the areas of: common communication strategy, legal and governance framework, dissemination of the future of European Research Infrastructures
EATRIS		Access to structural biology infrastructures and development of innovative approaches. Biomedical data to relate to molecular structure.	Comprehensive understanding of molecular and cellular structures and function for the development of improved or novel clinical products.	Use of technologies in structural biology for toxicology, functional genomics (metabolomics) structure-activity relationship and innovation in drug design
ECRIN		Biomedical data to relate to molecular structure	Biomedical research	INSTRUCT has been working together with all the BMS preparatory phase projects in the areas of: common communication strategy, legal and governance framework, dissemination of the future of European Research Infrastructures
ELIXIR		Identification and development of protocols for handling data derived from several infrastructures within INSTRUCT. Cross platform common data standards. E-Infrastructure for the deposition, curation, annotation, archiving and publishing of biomolecular structures and related data.	Support for integration of different structure determination technologies. Data management related to structure determination of proteins and complexes important in human health and disease	INSTRUCT and ELIXIR work closely to provide interoperability. There has been representation in related workpackages in each of the initiatives, as well as joint meetings.
Infrafrontier		<i>In vivo</i> assays of bioactive compounds. Functional data to relate to molecular structure and vice versa.	Structure/function of proteins for biomedical research	These infrastructures link together to allow investigation of systems spanning from molecule to organism.
EMBRC		Structure determination of novel molecules and their physicochemical dynamics.	Characterisation of novel molecules for biomedical and basic research.	EMBRC provides a source of novel molecules for structure determination in INSTRUCT
ERINHA		Data on pathogens to target for structural studies. Study of risk group 4 pathogens protein structure is often needed to better understand pathogenic mechanisms. Conversely, sample production from risk 4 group pathogens for structural study could be done in ERINHA.	Study of pathogen protein structure/function	INSTRUCT and ERINHA link together to offer the infrastructure required to characterise potential targets for therapeutics to combat pathogens
Euro-BioImaging		Correlative and structural imaging methods	Bridging resolution gaps of imaging methods. Identification of new imaging technologies to augment existing structure determination infrastructures.	Development of a common node for correlative light and electron microscopy
EU-Openscreen		Small molecules for analysis with protein structure information on mode of action of small molecules.	Information on potential protein targets and mechanisms of action of small molecules. Ultimately providing information underpinning novel drug design.	Infrastructures which will interface to bringing together proteins and their small molecule ligands
e-IRG		Data transfer, processing and curation	Data management	
SSH				
ESP				
ENV				
ENE				

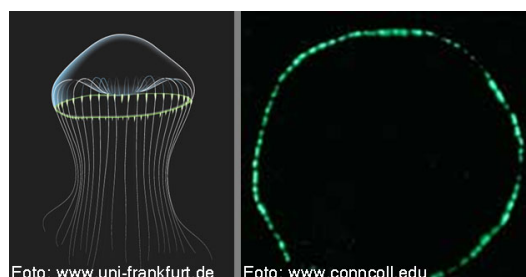


## 4.6 Descriptions of the 4 second generation BMS RIs

### 4.6.1 European Marine Biological Resource Centre (EMBRC)



The rationale for establishing a European Marine Biological Resource Centre (EMBRC) is to respond to the ever increasing demand for high quality provision of marine organisms to serve as models for research and development in diverse domains, ranging, for example, from global change to bio-fuel production. Marine organisms possess a plethora of unique biochemical pathways, biomaterials, physiological processes and genomic information, offering outstanding potential for bio-discovery in medicine, biotechnology and sustainable development (see Figure 24).



**Figure 24:** *Aequorea victoria* expressing green fluorescent protein

However, these opportunities remain largely untapped due to the currently fragmentary

nature of access to marine biological resources. By connecting existing marine biological research institutes located across the continent into a united organisation with common goals and strategies, Europe will take the leading role in structuring and driving forward marine biological research and technical development. This will involve mutualisation and coordinated development of state of the art facilities for the maintenance and provision of a coherently selected range of marine model organisms, as well as sophisticated technological platforms capable of delivering frontier science, in particular involving “-omics” approaches. Currently, a consortium of 12 of the leading European marine biological stations together with the European Molecular Biology Laboratory are ready to prepare for the construction and operation of the EMBRC in synergy with end-users and stakeholders who will be engaged in all aspects of strategic planning. This will include consideration of scientific, ethical, legal and socio-economic frameworks, and

the outcome of the proposal for the Preparatory Phase project will be a Memorandum of Understanding which is required to begin the construction of the EMBRC.

The expected impact of EMBRC beyond the field of marine biology is to enhance competitiveness of European research and industry in diverse contexts and to promote dissemination of environmental knowledge to policy-makers and the general public.

EMBRC was formally incorporated in the updated ESFRI Roadmap on 9<sup>th</sup> December, 2008. Immediately after this meeting planning began to incorporate new partners in areas where EMBRC was considered to have thin coverage and lobbying began by established partners to obtain letters of support from national and regional governments for the Preparatory Phase proposal, which was submitted on 3<sup>rd</sup> December, 2009.

### 1. Name and descriptive title

#### EMBRC - European Marine Biological Resource Centre

A consortium of the main coastal marine laboratories in Europe with a capacity to provide access to marine model organisms. EMBRC will act as a distributed infrastructure for high-level research in basic biology, marine biology and ecology including integration with modern technology and “-omics” platforms. The RI will provide and promote access to the infrastructure for marine biological researchers, for training the researchers of tomorrow as well as a resource for SMEs and industry. The RI will generate and lead outreach to stakeholders (both the public and industry).

### 2. Short description of new RI or major upgrade and main characteristics

EMBRC is designed to support the needs of the ERA in basic biology, marine biology and ecology and to foster its integration with other fields of sciences, including genomics and systems biology for the next 30 years. This infrastructure will also act as an incubator and “spin-off” for new ideas and technologies and will work with and alongside academics, SMEs and industry to apply these at the European level. Marine organisms are an essential component for our quality of life, for their contribution to the food chain and impact on the environment. However, given the difficulties in maintaining and culturing them they are the least well studied.

Marine models have provided experimental systems for seminal discoveries in basic science that impact on our quality of life in a concrete and lasting way (cf. Nobel prizes for physiology or medicine 1963, 1970, 2000, 2001). Thus, it is highly likely that marine organisms with their phylogenetic diversity offer access to presently unknown biological mechanisms which can in turn be used for biomedicine or for biotechnologies. **EMBRC** will be a distributed infrastructure comprising key coastal marine laboratories with complementary expertise and equipment providing i) access to marine laboratories, which encompass a representative set of European coastal ecosystems, fully equipped with modern boats, sampling devices and platforms in sequencing, transcriptomics, proteomics, metabolomics, structural biology and bioinformatics; ii) an integrated supply of key marine microbial, algal or animal organisms, as existing and new models for interdisciplinary marine biological research; iii) services from a central DNA and cell stock centre for marine model organisms, backed by dedicated platforms for the preparation of DNA libraries, cell lines and specific genotypes for functional genomics, including transgenic and mutant lines.

This infrastructure will build on and expand on the synergies developed in FP6 between the partners (see **Marine Genomics Europe** and **MarBEF** links below) and current activities in FP7 where several of the partners were funded to provide access to the RI under the **ASSEMBLE** programme.

#### Access:

Facilities are all currently accessible through mutual agreement and common projects (national or European). The infrastructure will provide seamless access to all sites and facilities for end-users.

#### Potential users:

**Marine Biologists** working on a wide range of interests from resource management, biodiversity, trophic structure to biotechnology and conservation biology. **Government and NGO Environmental Agencies**. **SMEs** with interest in biotechnology. **Researchers** using molecular biological and genomic approaches, in biomedicine, biochemistry, physiology, systematics, paleontology, ecology and research on global change and climate. **Companies** in aquaculture and those developing new materials, e.g. medicines and bio-fuels.

### 3. Scientific Case

Europe has a distinguished history in Marine Biology with its marine biological stations established in the late 19<sup>th</sup> century. They represented and represent a major European infrastructure that has acted to serve, enhance and develop collaborative marine research worldwide. Now, however, they have become a new breed of marine research stations, developing and applying new technologies and facilities that allow a higher quality of service, not only to the marine biological community but also to the increasing numbers of scientists that are turning to marine organisms as models with which to investigate fundamental questions in biology.

By providing access to fully equipped research laboratories next to coastal ecosystems, supplying access to living organisms and by carrying out their own in-house research programmes, marine research stations already act as Research Infrastructures for transnational access and, altogether, they represent a major asset for the European science community. Recent years have seen an increased interest in marine model organisms because of the emergence of cheap, rapid genome sequencing. The aim of integrating them will then be to capitalise on the complementarity and potential interoperability between marine institutes. The activity will primarily direct at “de-fragmenting” this set of infrastructures, by providing increased opportunities for research, access, collaboration and training. The outcome will be the creation of a major European distributed Research Infrastructure. In addition, the point must be made that in many instances, facilities and technologies need to be continuously improved. Among the vast body of necessary technological improvements, a number of joint research activities will be selected with the aim of maximising technological collaboration between sites. These actions will fall into three main categories: i) Improvement of instrumentation for access to the biodiversity of coastal ecosystems ii) Improvement of the production, maintenance, provision and utilisation of key marine models for biological sciences and iii) The functional analysis of ecological or biological models, using modern, systems biology approaches.

Transfer, expansion, improvement of quality and quantity of the newly developed technologies will involve a combination of workshops, practical courses and research with shared personnel. At the same time the links between SMEs, industry and research institutes will be addressed in **imaginative outreach programmes**. Physical restructuring will allow industrial and institutional partners to work alongside each other in new ways to provide new products outputs and solutions.

At the global scale this Infrastructure would provide one of the largest integrated marine biology platforms in the world, providing European scientists with cutting edge tools to address global issues. For a case pointing towards the creation of a European long-lasting, multi-site institute see the scientific challenges document (a position document on basic European Research in integrated Marine Biology supported by **Marine Biodiversity and Ecosystem Functioning (MarBEF)**, **European Network of Excellence for Ocean Ecosystems Analysis (EUR-OCEANS)**, and **Marine Genomics Europe (MGE)**). The issues of embedding this infrastructure appropriately into the ERA and international scientific landscape will be addressed by a specific work package in the Preparatory Phase of EMBRC.

### 4. Concept Case

Additional facilities are needed to integrate, marine biology and ecology with all areas of basic biological research. All the partners are arranged in a distributed infrastructure located by the sea and are equipped with model organism collection and maintenance facilities. The participants share state-of-art genomic and proteomic facilities.

- **Stazione Zoologica „Anton Dohrn“, Naples (SZN), Italy.** Sanger sequencing (medium throughput), robotic picking, spotting and analysis of microarray, real time PCR, Typhoon imaging.

- **Sven Loven Centre for Marine Sciences (previously KMRS and Tjarno), Sweden.** Real time PCR, proteomics (medium scale), culture collections.
- **Scottish association for Marine Science, Oban, UK.** Algal culture collections.
- **Station Biologique de Roscoff, France.** Algal culture collections, Sanger sequencing (medium throughput), robotic picking, macroarraying, HPLC-MS, GC-MS microarray/macroarray reading, protein expression and crystallisation, bioinformatics.
- **Observatoire Océanologique Banyuls sur mer, France.** Flow cytometry, imaging and platform for mass production of microorganisms. Access to “-omics” through Roscoff.
- **Observatoire Océanologique Villefrance sur mer, France.** Advanced microscopy and imaging, Sanger sequencing. Access to “-omics” through Roscoff.
- **Centro de Ciências do Mar (CCMAR), Faro, Portugal.** Fish cell lines, Sanger sequencing, Typhoon imaging, HPLC-MS, GC-MS.
- **Plymouth Marine Partnership, UK.** Led by The Marine Biological Association, (Plymouth Marine Laboratory, Sir Alistair Hardy Foundation for Ocean Science, and Plymouth University. Sanger sequencing and imaging.
- **Alfred Wegener Institute for Polar and Marine Research (AWI), Bremerhaven, DE.** High-throughput facilities, bioinformatics.
- **Institute of Marine Biology and Genetics (IMBG), Heraklion, EL.** High-throughput sequencing, “deep sequencing” facilities.
- **Sars International Centre for Marine Molecular Biology, (Sars), Bergen, NO.** High-throughput facilities.
- **European Molecular Biology Laboratory (EMBL), Heidelberg, DE.** Sequencing, bioinformatics, arraying.

#### **Additional technical infrastructure:**

1) **Upgrade** the capacity for holding, rearing and transporting marine model organisms, 2) **promote** the identification and establishment of new model organisms that are key players in ecosystems 3) **potentiate** the capacity to analyse genomes and gene expression profiles dedicated to marine organisms. 4) **disseminate** know-how and accessibility for these organisms and enable ecologists and basic biologists to work on them 5) **build** (where appropriate) modern adjacent laboratories and 6) **generate** new integrative departments. 7) **foster** transfer of knowledge between EMBRC and industry, including the development of science parks next to the basic research facilities. The planning of research resources will be addressed by a specific work package in the Preparatory Phase of EMBRC.

#### **5. Further information, including strategic importance to ERA**

This will be both a physical and virtual (e)-infrastructure. It will involve the development and physical expansion of the capacities of the marine institutes (this will be achieved by national, EU and industrial funding) to house and carry out research. This infrastructure will complement but not overlap with LifeWatch and ELIXIR (e-science and technology infrastructures for biodiversity data, observatories and data depositories) already on the ESFRI Roadmap and with which we are now actively setting up working groups. EMBRC **will not** emphasise the compilation and production of long-term data series and complex biodiversity data, instead it will seek to carry out strategic and basic high-level research which will underpin the EU knowledge base with the specific directive of addressing issues of improved quality of life and production. The data generated will feed into infrastructures (such as LifeWatch, ELIXIR and EBI, to unite the relevant systems biology information. The planning of e-infrastructure research resources will be addressed by a specific work package in the Preparatory Phase of EMBRC.

#### **6. Identification of other socio-economic impacts**

EMBRC marine stations are generally located in remote locations, or close to declining fishing or industrial harbours, where employment is an important issue. The EMBRC will provide a

stimulus for development of research and higher education activities in these maritime regions. Given the potential of “-omics” approaches for developing blue biotechnologies and new tools for resource management and conservation biology, it is fully expected that the EMBRC will also act as a catalyst for the establishment of spin-off industrial applications. Finally, EMBRC outreach activities to the general public should also help promoting tourism in these areas.

Based on its current partnership, EMBRC is envisioned as an enabling platform distributed across Europe, from north to south and east to west. It will be a driving force in structuring the ERA by providing access to resources and equipment to study the marine environment not easily available to scientists from most European countries. It will be open to enlargement of its membership to other countries, some of which have already expressed their interest. We will also take special care to consider early in our discussions (e.g. WP9 of the PP EMBRC proposal) the convergence and outermost maritime regions of Europe, particularly those from Bulgaria and Romania (Black Sea), as well as candidate Member States with important marine economies such as Iceland and Turkey.

#### **Training and recruitment:**

We are presently recruiting people for environmental genomics, metagenomics and bioinformatics. We plan to continue recruiting more people in these areas. We need to train and recruit the marine biologists of the future, integrating training in organismal biology, ecology and “-omic” sciences. This needs long-term planning and integration. This will be achieved by concerted recruitment in the key “-omic” areas, targeted PhD programmes and workshops. This is highly realistic, for example the partner SZN Naples runs an integrated PhD programme which trains marine biologists in both ecology and basic biology. This type of research school would become pan-European and targeted towards these high-throughput sciences. In particular, an international PhD programme in “marine systems biology and biodiversity”, currently involving 3 partners of EMBRC, is in preparation.

#### **7. Commitments/maturity: Which states/organisations have demonstrated interest/commitment in supporting and/or funding the proposal?**

This proposal builds on the already highly developed synergy between the partners of FP6 networks of excellence, Marine Genomics Europe and MarBEF and the ASSEMBLE I3 in FP7. Of the current partners in EMBRC (listed in section four), all the institutes have been and are currently working on joint network proposals, have a strong history of working together and have indicated possible funding interest through national schemes. At a recent meeting of the partners, it was estimated that, collectively, around 50 Mio € from national funds is planned for capital investment (mostly building labs and facilitates) within the next 5 years.

#### **Fitting the planned RI into existing facilities:**

The current infrastructure, through the process of convergence created by activities in current FP6 and RI activates in FP7, is already carrying out collaborative research in the area aimed at by the requested RI. However, we require upgrading of facilities (e.g., the ever decreasing cost of sequencing requires major investment in new technology), and we need to increase the functional capacity of the infrastructure. This process in itself opens up higher throughput and greater volumes of data which will need to be handled by computational biology techniques. No completely new facility is planned but the construction of new laboratories and of installations adjoining existing sites is envisaged.

#### **A history of sharing and cooperation that will be augmented by the RI:**

There is a tradition of sharing facilities and access in marine laboratories, which has been explicit since their inauguration in the 1880s'. Traditionally also, oceanographers have been used to close cooperation and collaboration because of the sheer size of their projects. Until recently, however, the community of marine biologists had remained very fragmented. Now we

are seeing a reawakening of this spirit of cooperation with the advent of the “-omic” sciences, which require equipment and analyses that are beyond the reach of single teams or even institutes. For the preceding reasons, this and earlier initiatives have been recognised by the partners as being timely. There is enormous scope for improving cooperation, particularly between biomedical scientists, biological marine biologists and ecologists. This is where we feel the new frontier in marine science is, and this would be here the major impact of this infrastructure.

#### **Support from national and regional governments:**

It is notable that support was obtained for the PP for all partners. During the lead-in to the PP EMBRC application the following states committed themselves formally to the PP: Italy, Sweden, Norway, France, UK, Scotland, Germany and Portugal. Formal support was also obtained from regional governments for the partners from Italy, Sweden, Norway, France, UK, Scotland, Germany, Portugal and Greece.

#### **8. Costs for construction, operation and decommissioning, indications on project financing.**

The key European marine laboratories involved are probably collectively worth more than 1000 Mio € in patrimonial value, and they are spending a total on annual operating costs of ca. 30 Mio €. With perspectives for higher and sustained funding, EMBRC will seek to markedly upgrade and improve the level of access to research facilities, provide and coordinate the supply of marine models and improve transnational access to coastal ecosystems. It will thus boost the efficiency of this unique infrastructure and further integrate the community of marine biologists. The costs indicated below are to be considered real costs for an effective upgrade.

Total preparatory cost	Total construction cost	Operation cost/year	Decommissioning cost
7.5 Mio €	100 Mio €	60 Mio €	Not applicable

#### **9. Timetable for construction, operation and decommissioning with duration and possible starting dates.**

**Preparatory phase.** An application was submitted for the Preparatory Phase of EMBRC (3<sup>rd</sup> December, 2009). The results of the request are not yet known. We have requested 5.5 Mio € from FP7 funds to cover the overall estimated cost of the PP of 7.5 Mio €. The PP EMBRC application contains mechanisms to 1) set up management and governing boards, 2) identify needs, identify strategic areas, and make concerted actions for the major capital initiatives. EMBRC will provide construction plans and will recruit and consult with stakeholders. We expect consultancy and planning of the infrastructure to take three years. To set up and run the EMBRC infrastructure would cost 7-10 Mio €. The EMBRC infrastructure will be managed by a governing board including the SZN and all other partners. A dedicated management team with an e-interface for the exchange and acquisition of data and information will be built to provide a unique access point for the distributed infrastructure. The interface will include inventories of available services and the modality of use of the infrastructure.

**Construction.** The construction phase will last 5 years and will involve the major costs of upgrading parts of the physical infrastructure and the purchase of new equipment. Using as an example the current IPs and NoEs, we calculate that 20 Mio € a year would be needed for 5 years from national/local and EU funds and equivalent from national and regional funds.

**Operation.** Full implementation of the infrastructure for ten year operation period. Beginning during the construction phase and tailing off during the decommissioning phase. Operation

costs are estimated as a fraction of current operating costs (ca. 30 Mio €/year). Hence if the national contributions to the operation of this infrastructure is currently 30 Mio €/year then a step-up in the activity level would require an additional turnover of 30 Mio € (15 Mio € supplied by EU sources and 15 Mio € by national funding). This would lead to an operating cost of 60 Mio € /year for the time course of the operation phase.

**Decommissioning.** It is envisaged that once the infrastructure has been demonstrated to be functional and productive, its long-term function will be maintained by national funding and industrial sponsorship, with a relatively small input from the EU. European marine stations have grown and have been maintained for almost 140 years, in this new phase they will transform into a major European infrastructure with long-term prospects and thus in the future we would not expect there to be any major decommissioning costs.

Preparatory phase 2010-13	Construction phase 2012-17	Operation 2014-34	Decommissioning Not applicable
------------------------------	-------------------------------	----------------------	-----------------------------------

**10. Reference: Person who has submitted the proposal and will follow up in ESFRI.**

Prof. R Di Lauro  
Stazione Zoologica Anton Dohrn  
Villa Comunale, 80121 Napoli, Italia  
Tel 0039 200815833  
Fax 0039 200817641355  
Email: [dilauro@szn.it](mailto:dilauro@szn.it)

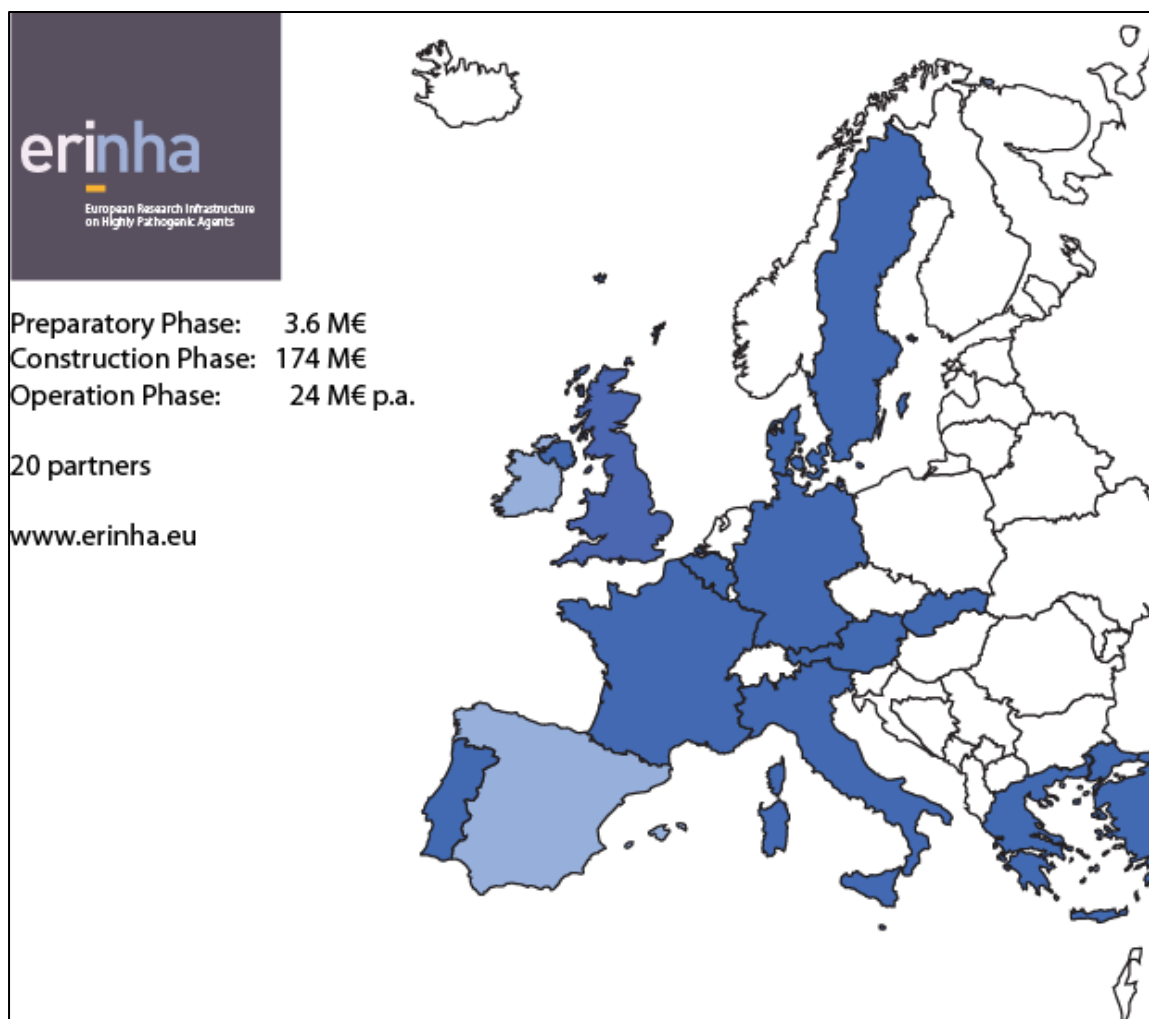


**Table 13:** Links between Research Infrastructures – EMBRC

	EMBRC	Further specification of the technological link	Further specification of the thematic link	Short statement for further specification (last update February 2010)
BBMRI	↔	New model organisms for biological and biomedical research could be referenced here	Biobanking opens resources to users beyond marine biology	Potential biobanking of marine model organisms for reference
EATRIS	↔	Means (pipelines) to test and provide access to new marine based medicines		New medicines
ECRIN				
ELIXIR	↔	Data storage and serving standards and benchmarks	marine organisms 'omic' data served and made available to a wider scientific public	Data serving of genomic data and provision of bioinformatic resources
Infrafrontier				
INSTRUCT	↔	Determining the structures of novel molecules and their physiochemical dynamics	Molecules for biomedicine and basic research	Structural biology of novel molecules
ERINHA				
Euro-BiolImaging	↔	Use and testing of novel imaging technology	Imaging in marine biology	Application and testing of novel imaging technology
EU-Openscreen	↔	Testing and provision of novel marine products for bio-medicine	Novel natural products	Testing and provision of novel marine products for biomedicine
e-IRG	↔	Infrastructure to serve and integrate distributed RI application of new technologies	Application of e-infrastructure to link components of the RI this has a broader scope than the data serving activities with ELIXIR	Application of e-infrastructure to link components of the RI this has a broader scope than the data serving activities with ELIXIR
SSH				
ESP				
ENV	↔	Bringing new technologies and models to help answer key environmental questions	Interactions with LifeWatch and other ENV RIs	Interactions with LifeWatch and other ENV RIs
ENE		Potential interaction over novel biofuels		Potential interaction over novel biofuels



#### 4.6.2 European Research Infrastructure on Highly Pathogenic Agents (ERINHA)



In the context of the emerging and re-emerging infectious diseases involving highly pathogenic microorganisms, European countries have to be well prepared to face such threats. However the Biosafety Level 4 (BSL4) capacity in Europe is not sufficient enough to cover the efficient development of diagnosis, prophylactic and therapeutics means against these pathogens. Moreover, there is no global coordination of activities and harmonization of practice in this field. Therefore the ERINHA initiative proposes the creation of a top world-class BSL4 Research

Infrastructure that will address the actual capacity sparseness. The project plans to conduct five main actions: i) Building additional BSL4 areas on several existing BSL4 laboratories (see Figure 25), ii) Building BSL4 laboratories in strategically selected EU countries that are lacking one, iii) Building support infrastructure around BSL4 laboratories mainly dedicated to host scientific visitors and staff, iv) Organising the users access to ERINHA infrastructure, v) Establishing coordination capacities for efficient dispatching and control of all activities.



**Figure 25:** Biosafety Level 4 Laboratory

During 36 months, the ERINHA Preparatory Phase will focus on i) Political and financial commitments from national, European or international concerned entities to support

construction, ii) Identification of relevant sites in Europe for new BSL4 construction or major upgrades, iii) Establishment of a secured and validated financial plan for construction, iv) Definition and implementation of an appropriate governance and legal framework, v) Harmonisation, standardisation and dissemination of SOPs related to L4 biological resources management, biosafety and biosecurity issues, iv) Definition and implementation of standardised training programmes for operating in BSL4 facilities, vii) Identification of ERINHA's users and organisation of users access rules. These achievements will allow ERINHA project to reach the legal, financial and technical maturity to move to construction phase.

### 1. Name and descriptive title

## ERINHA - European Research Infrastructure on Highly Pathogenic Agents

### 2. Short description of new RI or major upgrade and main characteristics

In the context of the emergence and re-emergence of infectious diseases involving highly pathogenic microorganisms, there is a crucial need for Europe to be well prepared to face any pandemic threat. It is thus necessary for European countries to have enough BSL4 laboratories at one's disposal to fully manage diagnosis and development of prophylactic and therapeutics means against these types of pathogens. European BSL4 capacities have been poorly developed, even if recent efforts have been made to face potential bioterrorist attacks.

In this context, there is a real need to create an adapted and coordinated pan-European BSL4 task force in order to face any BSL4 classified pathogen related pandemic. Objectives of such pan-European task force are to increase the: development of diagnosis, basic and finalised activities, biological resources management and training activities.

To reach these objectives, the initiative proposes to create a task force by conducting **five main actions**:

#### To build additional BSL4 areas on existing sites

The first one concerns the building of additional BSL4 areas on already existing BSL4 laboratories sites. The building of these new areas will permit to create and manage biological resource centre as recommended by OECD ([www.oecd.org/document/36/0,3343,fr\\_2649\\_34537\\_3877720060\\_1\\_1\\_1\\_1,00.html](http://www.oecd.org/document/36/0,3343,fr_2649_34537_3877720060_1_1_1_1,00.html)) to separate diagnosis activities from basic research and R&D ones, to include capacities to work on bacteria and to increase animal facility capacities. All the existing European BSL4 laboratories will be involved in this action.

#### To build new BSL4 structures

Italy (National Institute for Infectious Diseases L. Spallanzani, Istituto Di Ricovero e Cura a Carattere Scientifico (IRCCS), Rome), Germany (Bernhard Nocht Institute for Tropical Medicine, Hamburg; Robert Koch Institute, Berlin) and Netherlands (National Institute for Public Health and the Environment (RIVM), Bilthoven) are planning to build new BSL4 laboratories and are involved in the initiative.

Since most of existing or planned BSL4 laboratories are located in Western Europe (United Kingdom, Sweden, Germany, Italy and France), the building of two more BSL4 laboratories in Eastern Europe (for example: Poland, Austria) will be examined.

#### To build support infrastructure

In order to help European countries that do not have BSL4 capacities to participate to the fight against BSL4 classified pathogens, it is of main importance to give access to such infrastructure to scientists from these countries. Moreover, at present time, most operators or on site users of BSL4 laboratories are mainly virologists belonging to the basic research community. However, it is clear that to solve health problems related to infectious diseases a multidisciplinary approach, involving for example academic immunologists and other community such as industry is needed and that more research teams need to have access to BSL4 facilities. Capacities to host scientific visitors in terms of experimental areas outside BSL4 laboratories and offices are needed. The building of such infrastructures in existing or future BSL4 laboratories will be included in the creation of ERINHA infrastructure.

#### To organise the users access to the ERINHA infrastructure

To ensure that the infrastructure is efficiently exploited by the European scientific community, the access to the infrastructure will be organised and access rules will be defined.

#### To create coordination capacities

To avoid any redundant activities, to promote efficient collaborations and to facilitate exchange of information and experience, a specific body in charge of the coordination of all the activities related to highly pathogenic agents at the European level will be created.

### **3. Scientific Case**

#### Health context

Several emerging and re-emerging infectious diseases including viral haemorrhagic fevers such as Ebola, viral encephalitis like Nipah and others could have a major burden on socio-economic development in the developing countries and through migrations and global travels increasingly threaten the population of Europe as well. These microorganisms highly pathogenic for humans are classified as biosafety level 4 (BSL4) pathogens and must be handled in high-security BSL4 laboratories.

Until now, only BSL3 pathogens such as SARS and avian flu epidemics have represented worldwide threats. But these emergences have demonstrated the reality of the infectious threat and our vulnerability in front of emerging or re-emerging infectious diseases. Moreover, the reality of the bioterrorist threat which includes the use of highly pathogenic micro organisms, such as BSL4 pathogens, must also be taken into account.

Finally, BSL4 classified pathogens are only, at the current time, represented by viruses and all BSL4 laboratories are designed and equipped for the handling of viruses. Yet, many experts do not exclude that within the near future other emerging microorganisms such as multi-resistant bacteria (like *Mycobacterium tuberculosis*) could be classified as BSL4 pathogens. This would lead to main modifications in the organisation and equipment of all the BSL4 laboratories.

#### Definition of the needs

In this context, the scientific challenges are enormous and the survey and study of these agents are needed. The implementation of such strategy implies the development of diagnosis, basic and finalised research activities.

Diagnosis is essential for survey and characterisation of the pathogen as well as for the constitution of a collection. Basic research is of great importance for definition of therapeutic and prophylactic targets and finalised research is necessary for the development of diagnostic, prophylactic and therapeutic tools. Specific training of all BSL4 users is also of importance to ensure maximum biosafety conditions. Finally, the constitution of BSL4 pathogens collection is essential for the achievement of all the activities cited below. All these activities are closely linked and to reach the needed high international level of excellence, each member must be able to cover all of them, in the highest quality manner.

At the present time it is very difficult to define precisely the needs in terms of infrastructure and a clear assessment in this field will be needed. However, we have learned from the recent avian flu and Chikungunya outbreaks. The first lesson has been that the disposal of diagnosis capacities was not sufficient to solve the problem. Indeed, after identification of these pathogens, it has been necessary to initiate research programme to try to develop prophylactic and therapeutic means. Concerning the Chikungunya outbreak in "La Reunion", more than 10 BSL3 laboratories, including animal facilities, have been activated, in France only. Even though the virus has only threatened the south part of Europe, BSL3 laboratories have been solicited

all over Europe. In the case of H5N1 threat, even if no human cases have been detected in Europe and no inter human contamination demonstrated, over 20 BSL3 laboratories had to work on the virus.

Moreover, capacities for testing new vaccine or new therapeutics tools on animal models remain insufficient since for example only one BSL4 laboratory in Europe (Lyon, France) has the capacities to work on non human primate models.

Another issue has to be taken into account: each 12 or 18 month BSL4 facilities have to be closed for approximately 2 months for global maintenance, limiting then the capacity of activities.

Taking into account all these remarks, it seems clear that with only few number of BSL4 laboratories Europe would not be able to face a real BSL4 classified pathogen pandemic situation. Thus, there is a crucial need to have more BSL4 spaces and also experts available. Most of the existing BSL4 laboratories host only research and diagnosis activities and lack biological resources management and training capacities. It thus implies building of additional BSL4 areas for implementation of all activities including increased hosting capacities. Moreover, BSL4 laboratories are located within Western Europe and even if it is of interest to provide with such infrastructures one more western country like Spain, a broader distribution of these infrastructures involving one or two more BSL4 laboratories in Eastern Europe would also be very efficient for fighting infectious diseases.

#### Potential users

Most users or operators of existing BSL4 laboratories are virologists who belong to the basic research community. It seems of major importance to be in situation to develop adapted scientific programmes that scientists belonging to other scientific specialties such as immunologists or chemists and to other community like industry can have access to BSL4 facilities. Of course access must be given, under specific security processes, at the international level.

#### Conclusion

To conclude, it is virtually certain that as the creation of BSL3 facilities and networks for the study of HIV in the 80s led to major scientific discoveries, the increase in BSL4 laboratories capacities and the reinforcement of coordination efforts will have a major impact on our knowledge of high pathogen infectious mechanisms and on health progress.

The ERINHA infrastructure, described in the proposal, will permit to address scientific urgent questions in term of diagnosis, prophylaxis, therapy and to face efficiently the emergency of new viruses.

### **4. Concept Case**

The 5 main actions that are proposed to reach our objectives (to increase research, diagnosis, management of biological resources and training capacities of the European BSL4 laboratory network) concern the building of new BSL4 area on existing BSL4 infrastructure sites, the building of new BSL4 laboratories, the building of support infrastructures and the creation of a European coordination body.

#### The conceptual design of a BSL4 laboratory

Each BSL4 laboratory needs to be designed and scaled to host the four main activities needed to fight infectious diseases: diagnosis, microorganisms collection, research and training. All these activities cannot be performed in the same area. Diagnosis activities must be separated from research to avoid any false diagnostic results that could be generated through sample

contamination with concentrated viral preparation used for research activities. Moreover, since no efficient manufactured diagnostic tools are available for BSL4 pathogens, the diagnostic room must also be designed to integrate GLP (good laboratory practice) standards for the production of reagents. Since diagnostic activity will generate additional strains and because collection must also be protected from any contamination, the collection room must be closely linked to the diagnostic room. The research units must be designed to accommodate at the same time experiment involving different microorganisms. Because research units are used for research activities and also for training, it has also to be scaled and equipped with enough emergency exits to avoid limiting accesses. Animal facilities can be directly linked to research unit and must be scaled and designed to house all pertinent and permitted animal models.

Of course, activities involving BSL4 pathogens are very dangerous and sensitive, and each BSL4 laboratory holder has to define and set-up specific security plans. Security is one of the expertises that will be shared and implemented between all BSL4 units. This implies to create a specific workpackage in charge of security aspects which will be shared with all new participants.

In each case international standards will constitute the references for conception of new BSL4 areas as well as for quality, biosafety and biosecurity management. International guidelines such as the WHO guideline for the safe transport of infectious pathogens ([http://www.who.int/csr/resources/publications/WHO\\_CDS\\_CSR\\_LYO\\_2004\\_9/en/](http://www.who.int/csr/resources/publications/WHO_CDS_CSR_LYO_2004_9/en/)), the Laboratory Biosafety Manual Third Edition ([http://www.who.int/csr/resources/publications/biosafety/WHO\\_CDS\\_CSR\\_LYO\\_2004\\_11/en/](http://www.who.int/csr/resources/publications/biosafety/WHO_CDS_CSR_LYO_2004_11/en/)), the Centers for Disease Control and Prevention (CDC) biosafety guideline (<http://www.cdc.gov/od/ohs/biosfty/biosfty.htm>) or the recommendation guideline for biological resource centre edited by OECD ([http://www.oecd.org/document/36/0,3343,fr\\_2649\\_34537\\_3877720060\\_1\\_1\\_1\\_1,00.html](http://www.oecd.org/document/36/0,3343,fr_2649_34537_3877720060_1_1_1_1,00.html)) will be used in the conception, building and management of the new BSL4 infrastructure.

#### Building of additional BSL4 areas on existing sites

For each existing laboratory an analysis of the capacities will be performed and compared to the needs before a proposal is established. For each, addition of diagnostic room, Bioinformatics Research Centre (BRC) room, research area and animal facility will be studied. National regulation will always be taken into account.

#### Building of new BSL4 structures

Concerning the building of new BSL4 laboratories, the project will integrate all the new design and organization concepts gained from the past experience of current holders, including the integration of capacities for animal models development.

#### Buildings support infrastructure

In each involved institute a specific study for building of support infrastructure will be performed. The study will take into account needs in term of space, but also specific needs to host multi-disciplinary research teams.

#### Organising the users access to the infrastructure:

The access organisation to the ERINHA infrastructure will be defined for partners and external users. It will rely on the elaboration of access rules which will be based on the evaluation of the partners and external users' needs. Drafts of agreement related to access rules between countries will be elaborated.



### Creating coordination capacities

This RI will of course need the implementation of centralised external governance that will have to coordinate the activities. The coordination in case of pandemic outbreak is of main importance since it will lead to an efficient dispatching and control of all activities required to face such situation. For this, a management structure including a steering committee and a scientific advisory board will be implemented. During the Preparatory Phase an additional and specific project team, including a dedicated project manager, will be created. Organisation of specific workpackages in charge of management of experimentation, diagnosis, biosafety, security, ethic, legal and societal issues. Of course the coordination body will set up strong links with the European Centre for Disease Prevention and Control (ECDC) for the management of BSL4 classified pathogens related outbreak.

It is of note that European coordinated networks concerning high-security facilities (European Network of P4 laboratories (EURONET-P4/ENP4Lab), European Training for Infectious Disease Emergencies (ETIDE), European Network for Diagnostics of "Imported" Viral Diseases (ENIVD)) have now been created. ENP4Lab, that has replaced EURONETP4 (<http://www.euronetp4.com/>), is a European Union project sponsored by the DG-SANCO Public Health programme that networks European BSL4 laboratories. It aims to enhance cooperation, communication and exchange of information between BSL4 laboratories in Europe with a specific focus on biosafety and biosecurity issues and diagnosis activities. Since that project gathered all existing and future BSL4 laboratories, it could constitute the frame of the coordination body.

Moreover, biobanking and investigation of samples that may contain BSL4 pathogen is essential to study pathogen host interaction as a basis for new diagnostics and therapies. In this way and collaboration with the Biobanking and Biomolecular Resources Research Infrastructure (BBMRI, <http://www.bbMRI.eu>) a concept will be developed for biobanking of human biological samples containing high risk pathogens.

The distributed European infrastructure will not work with complementary BSL4 units but will take advantage of distributed competences and expertises in all the European space.

### **5. Further information, including strategic importance to ERA**

In the frame of a European BSL4 network constitution, sharing information and harmonising processes are essential. In this view, three actions could be developed:

1. Harmonisation of the internal information management processes, particularly in the fields of the quality assurance, the biosafety and biosecurity risk assessment;
2. Standardisation of the identification and the description of the biological material in order to provide data through common description formats and standard exchange files (e.g. eXtensible Markup Language (XML)) for classified and free access catalogues;
3. Creation of an e-infrastructure, with different levels of security including highly secured level for BSL4-authorized-staff only, which gives, among other data, the availability of diagnostic rooms and animal facilities of the network members, in case of emergency.

Of course, exchanging all information, especially those classified as sensitive or confidential, through e-infrastructure is difficult but possible to secure. However, all activities and related information conducted in BSL4 laboratories do not need highly secured exchange channels. Taking into account all these features, an efficient service oriented e-infrastructure for the BSL4 network can equip European Research Infrastructures with a unique virtual BSL4 facility.

Existing websites would be, of course, invited to join the network, e.g. EURONET-P4 website (<http://www.euronetp4.com/>).

## 6. Identification of other socio-economic impacts

The health sector is one of the main economic sector and large investments are made to fight diseases on a global scale. In this field, infectious diseases control is one of the main challenges which requires the development of new drugs, vaccines, and diagnostics tools.

As explained below, the main missions of such infrastructures can be divided into 4 categories, diagnosis, research, biological resources management and also training. Training of people that will work in such laboratories is of great importance since each action to be done can have major health consequences and must then be previously calculated and described in a specific procedure guide. Training of people implies also that time and space must be available and managed. To reach such objectives broad and well organised BSL4 area must be available. It includes the separation of research activities from diagnosis and resource management ones.

Concerning involvement of industries, it is of note that, the close relationship that currently exists between some existing BSL4 structures in Europe and health industries has demonstrated its capacity to help industrial development as well as the crucial role it plays in the success of these developments. This acquired experience should be useful to reinforce and increase the collaborations between research and industrial actors of the domain. To facilitate and encourage such associations an increase in infrastructures and biological resources circulation capacities would be of first importance.

## 7. Commitments/maturity: Which states/organisations have demonstrated interest/commitment in supporting and/or funding the proposal?

Europe has already a history in the study of highly pathogenic microorganisms as demonstrated by the existence of BSL4 laboratories in some European countries, by networking activities in that field and edition of guidelines as well as exchange or information for the management of biosecurity and biosafety issues.

### Existing European Infrastructures

There are 6 identified existing running BSL4 laboratories in Europe that are classical partners of European networks. The first ones were constructed in UK (Porton Down, <http://www.hpa.org.uk/cepr/specialpathogens/default.htm>) and Germany (Marburg and Hamburg). Within the 90s 3 other countries have built such facilities, France with the Inserm Jean Merieux P4 Laboratory in Lyon, Italy in Rome at the L. Spallanzani hospital and Sweden in Solna at the Swedish Institute for Infectious Disease Control. **All of them are supported by governmental funds.**

### Future BSL4 laboratories already planned

Moreover, in front of emerging infectious diseases threat some European countries already planned to build new BSL4 laboratories within the coming years. In Italy, a large BSL4 infrastructure including clinical facilities to house and treat infected patients and a BSL4 laboratory is under construction at the L. Spallanzani IRCCS in Rome to replace the existing one. In Germany, a new BSL4 laboratory is under construction in Hamburg at the Bernhard-Nocht-Institute for Tropical Medicine to replace the small old one, and the building of a new one is planned in Berlin at the Robert Koch-Institut. **The building of all these new infrastructures is supported by governmental funds.**

### Networking activities

Since 9/11 and more recently with the SARS and avian flu emergencies European countries as other countries all over the world have realised that highly dangerous microorganisms emergency can represent a serious threat. Concerning BSL4 classified pathogens, this

awareness has led to the creation and funding in 2004 for 3 years of a BSL4 laboratory network entitled (<http://www.euronetp4.com/>). This action has been renewed for 3 more years in 2007 through the funding of ENP4Lab. The main outcomes consisting in harmonisation and standardisation of practices within biosafety and biosecurity domains to ensure a better interoperability and comparison of results. The partners of the project are Italy (National Institute for Infectious Diseases L. Spallanzani IRCCS, Rome), Germany (Bernhard-Nocht-Institute for Tropical Medicine, Hamburg, Philipps-Universität Marburg, Marburg), United Kingdom (Health Protection Agency, London), Sweden (Swedish Institute for Infectious Disease Control, Solna) and France (National Institute for Health and Medical Research, Lyon). Observers have also been integrated in this project (Österreichische Agentur für Gesundheit und Ernährungssicherheit Spargelfeldstraße 191, Wien, Austria, Robert Koch-Institut, Berlin, Germany, National Institute for Public Health and the Environment (RIVM), Bilthoven, Netherlands). Within the recent past, other networking project (ETIDE; ENIVD) mainly focusing on the diagnosis of BSL4 classified pathogens were funded by EU. ETIDE (<http://www.etide.eu/default.aspx>) project funded by the DG Health and Consumer Protection since 2006 for a 3 years period aim to produce a training programme and training materials specifically to enhance European capacity to recognise and respond effectively and in a coordinated fashion to infectious disease emergencies. The ENIVD project (<http://www.enivd.de/index.htm>) funded by the DG SANCO aims to exchange and gather information that can improve the diagnostics of "imported" viral diseases in Europe. Members of the ENP4Lab network participate to these 2 EU projects.

#### Guidelines for biosafety and biosecurity issues:

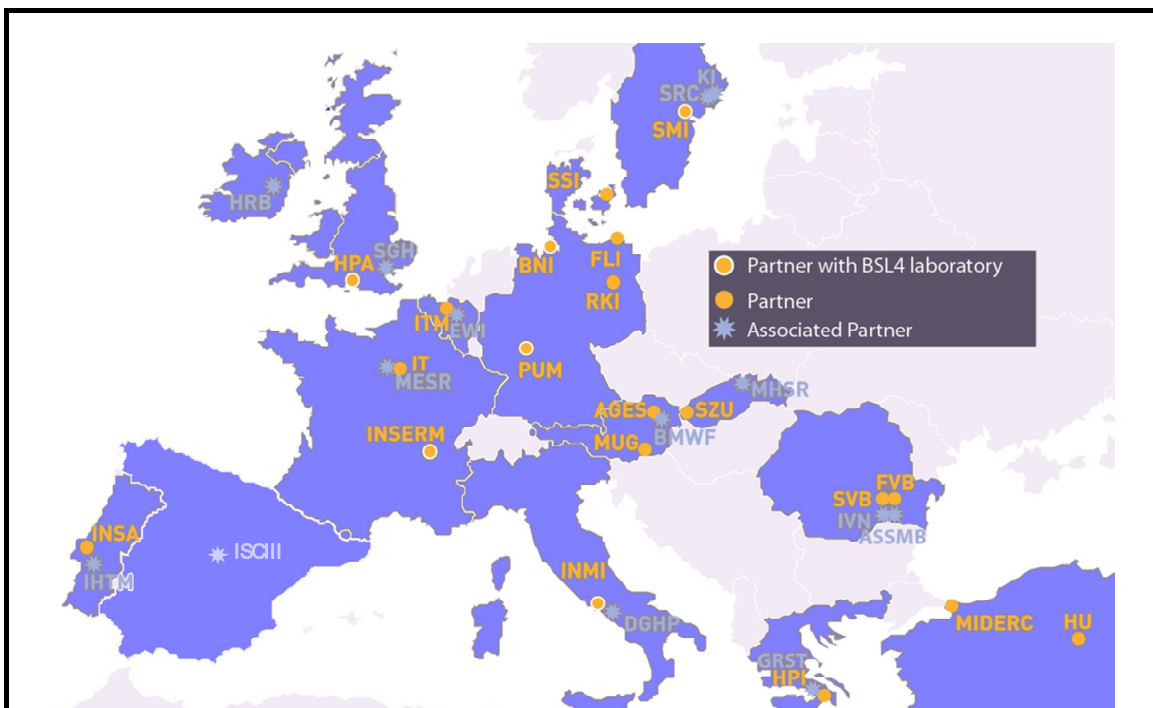
Since activities involving BSL4 pathogen are very dangerous and sensitive, each BSL4 laboratory holder has been obliged to define and set up specific security plans. All these plans have been based on recommendations included in international guidelines such as the WHO guideline for the safe transport of infectious pathogens ([http://www.who.int/csr/resources/publications/WHO\\_CDS\\_CSR\\_LYO\\_2004\\_9/en/](http://www.who.int/csr/resources/publications/WHO_CDS_CSR_LYO_2004_9/en/)), the Laboratory Biosafety Manual - Third Edition ([http://www.who.int/csr/resources/publications/biosafety/WHO\\_CDS\\_CSR\\_LYO\\_2004\\_11/en/](http://www.who.int/csr/resources/publications/biosafety/WHO_CDS_CSR_LYO_2004_11/en/)), the CDC biosafety guideline (<http://www.cdc.gov/od/ohs/biosfty/biosfty.htm>), or the recommendation guideline for Biological Resource Centre edited by OECD ([http://www.oecd.org/document/36/0,3343,fr\\_2649\\_34537\\_3877720060\\_1\\_1\\_1\\_1,00.html](http://www.oecd.org/document/36/0,3343,fr_2649_34537_3877720060_1_1_1_1,00.html)).

Of course security expertises have been gained by the past by all BSL4 laboratory holders and will be shared by all future BSL4 units.

#### Organisations that have demonstrated interest in supporting the proposal:

All institutes holding BSL4 laboratories are concerned by this initiative and have been contacted. Most of them, like the National Institute for Public Health and the Environment (RIVM) in Bilthoven (Netherlands), the Health Protection Agency in London (United Kingdom), the Swedish Institute for Infectious Disease Control in Solna (Sweden), the "Österreichische Agentur für Gesundheit und Ernährungssicherheit Spargelfeldstraße" in Vienna (Austria) and the National Institute for Health and Medical Research in Lyon (France) have expressed their interest in this proposal. Some others that have already build or are building new BSL4 laboratories like the Bernhard-Nocht-Institute for Tropical Medicine in Hamburg (Germany) or the National Institute for Infectious Diseases L. Spallanzani IRCCS in Rome (Italy) are mainly interested in the networking activities included in the proposal.

ERINHA now gathers relevant and complementary expertise of key partners and associated partners from 15 countries across Europe, including all 6 identified existing running BSL4 laboratories, research institutions and national ministries, as well as key personnel and organisations from BBMRI (of course, all other key stakeholders not yet identified would be integrated in the project during Preparatory Phase).



**Figure 26:** Overview of ERINHA Partners

Three European countries, Italy, Germany and the Netherlands have already committed funds to build new BSL4 structures. All the countries that have or plan to have BSL4 laboratories have committed to ensure operation cost of their national infrastructure (see Figure 26).

## 8. Costs for construction, operation and decommissioning, indications on project financing.

### Preparatory cost:

For the 3 years of Preparatory Phase a team of 3 permanent people including a senior scientist as project manager, an engineer and a secretary will be constituted. Consultation of architects and consultants firms will also be needed. The estimated cost of this phase is 4.4 Mio €.

### Construction cost:

The estimated surface area that will be added to existing BSL4 laboratories is 100-200 m<sup>2</sup>. The one for new BSL4 laboratories including all activity capacities is 350 m<sup>2</sup>. Based on our recent experience, the construction cost of a 100-200 m<sup>2</sup> BSL4 facility is 10 Mio € and the one of a 350 m<sup>2</sup> BSL4 facility is estimated at 15 Mio €. Thus, for the construction of additional BSL4 areas to existing BSL4 laboratories the cost will represent 60 Mio € (6x10 Mio €), for the construction of new BSL4 laboratories the cost will reach 90 Mio € (6x15 Mio €).

The estimated construction cost of support infrastructures to existing and future BSL4 laboratories is 24 Mio € (12x2 Mio €).

### Operation cost:

The operation cost of the French 200 m<sup>2</sup> BSL4 laboratory, excluding experimentation cost, is 2 Mio €/year. The total operation cost for 12 European BSL4 laboratories will thus be 24 Mio €/year.

Total preparatory cost	Total construction cost	Operation cost/year	Decommissioning cost
(of which already spent or committed)	(specify contributions committed or indicated by possible funders)	(specify contributions by possible funders)	(possible funders)
4.4 Mio €	174 Mio € (50% from national funds)	24 Mio € (60% from national funds and 20% from private funds)	

**9. Timetable for construction, operation and decommissioning with duration and possible starting dates.**

Preparatory phase

During the Preparatory Phase, a detailed evaluation of needs for each existing and future BSL4 infrastructures will be performed. It will be followed by a design study phase of new BSL4 areas including financial aspect. At the same time the coordination body, including centralised small groups for coordination, will be defined and implemented. Finally, consultation of stakeholders will be performed. The duration of this phase, based on our experience gained during the building of existing BSL4 is estimated to be 3 years.

Construction phase

The construction phase will include the building of new BSL4 areas and support infrastructures but also the validation of all new area and laboratories. The operational validation of BSL4 laboratories, that include technical validation of the infrastructure but also implementation of all procedures, is a very important and obliged step before obtaining all authorisation to operate the infrastructure. It can represent the longest step of the construction phase. As an example, the French BSL4 laboratory in Lyon has been built in one year but the authorisation to operate has been obtained over 2 years later. The estimated duration for the construction phase in this project is 5 years.

Operation phase










Since BSL4 laboratories are regularly maintained and upgraded when needed, there is no reason to limit the operation phase.

Preparatory phase 36 months	Construction and validation phase 60 months	Operation	Decommissioning
--------------------------------	--	-----------	-----------------

**10. Reference: Person who has submitted the proposal and will follow up in ESFRI.**

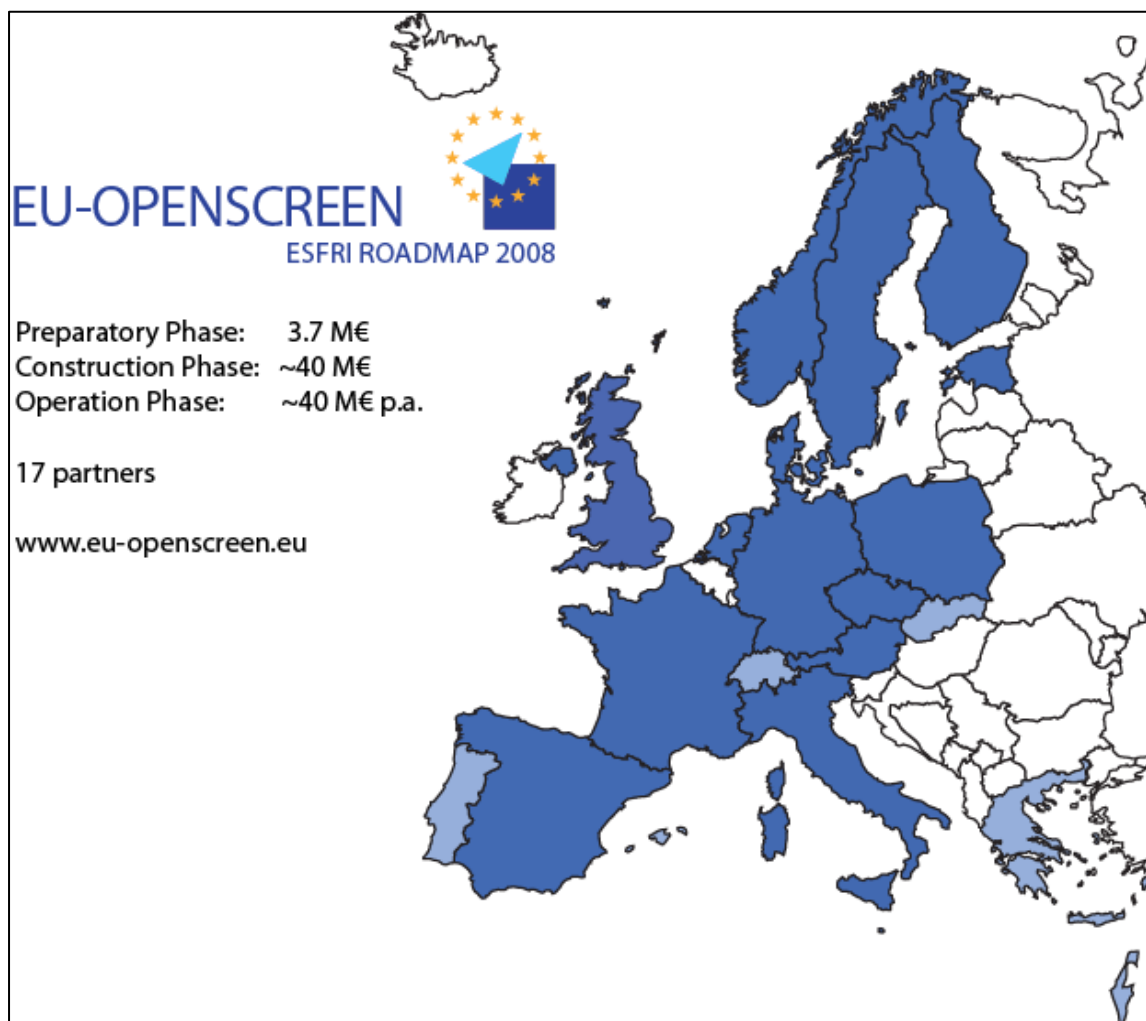
Hervé RAOUL  
LABORATOIRE P4 Inserm JEAN MERIEUX  
21 avenue Tony Garnier  
69365 Lyon cedex 2007, France  
[hervé.raoul@inserm.fr](mailto:hervé.raoul@inserm.fr)  
<http://www.cervi-lyon.inserm.fr>

**Table 14:** Links between Research Infrastructures – ERINHA

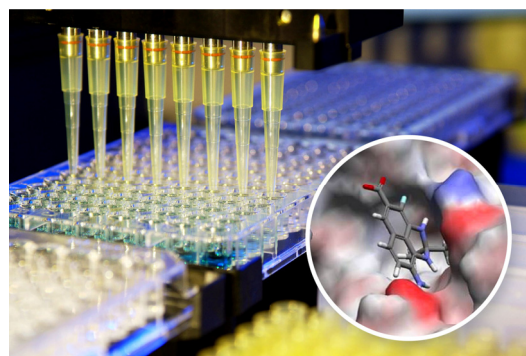
	ERINHA	Further specification of the technological link	Further specification of the thematic link	Short statement for further specification (last update February 2010)
BBMRI		Link between BBMRI and ERINHA in the establishment and management of sample collections and biorepositories associated with BSL4 laboratories; and in the harmonisation of quality, biosafety, biosecurity procedures for work with biohazardous samples including material handling and exchange within collection and repository centres	Biological resources centres	Establishment and management of biological sample collection
EATRIS		ERINHA will be the European structure where antimicrobial drugs efficacy can be tested on living risk group 4 pathogen. This include those developed by EATRIS	Development of antimicrobial products	
ECRIN		Preclinical experiment test will be done and data will be produced using ERINHA and should constitute an input for development of clinical test that could be performed through ECRIN.	Development of antimicrobial products	
ELIXIR		Linking biomedical and biological data resources will facilitate the understanding of diseases and lead to improved disease management and preventive strategies. ERINHA could contribute to the implementation of a database of biological material from experiments conducted in BSL4 laboratory, hosted through ELIXIR.	Biological information	Biological material database implementation
Infrafrontier				
INSTRUCT		Study of risk group 4 pathogens protein structure is often needed to better understand pathogenic mechanisms. In this view access to INSTRUCT will be of main interest for ERINHA. On the other hand, production of proteins from living risk group 4 pathogens for structural study to be perform in INSTRUCT could be done in ERINHA.	Protein structure study	
EMBRIC				
Euro-BiolImaging		Capacities development of cell and tissue imaging adapted to the needs of BSL4 laboratories	Cell and tissue imaging	Capacities development of cell and tissue imaging adapted to the needs of BSL4 laboratories
EU-Openscreen		ERINHA will be the European structure where antimicrobial drugs efficacy can be tested on living risk group 4 pathogen. This include those identified through prescreening by EU-openscreen. Some screening test that requires BSL4 containment could be done through ERINHA.	Chemical resources	Identification of targets/leads
e-IRG		High capacity of e-data storage and analysis for ERINHA, with different level of access security	E-data storage and access	High capacity of data storage and analysis, with different level of access security
SSH				
ESP				
ENV		In the field, sampling activities are often needed for epidemiological survey. For risk group 4 pathogens, part of the analysis of the samples could be done using ERINHA.	Epidemiological survey	Epidemiological data sources
ENE				



#### 4.6.3 European Infrastructure of Open Screening Platforms for Chemical Biology (EU-OPENSREEN)



The EU-OPENSREEN Preparatory Phase forms the basis for the construction and operation of a pan-European infrastructure of open screening platforms for Chemical Biology. EU-OPENSREEN will bring together leading laboratories from 12 European countries covering all aspects of chemical biology from high-throughput screening with a dedicated compound library to assay development, chemical synthesis for hit-optimisation, bio-profiling and *in vivo* studies (see Figure 27), as well as a central database, training for scientists and platform staff and dissemination activities.



**Figure 27:** Screening of bioactive small molecules

The infrastructure will be used by researchers from universities, research institutes and SMEs across Europe, who either have only limited in-house facilities or no access at all to such resources and expertise. The EU-OPENSREEN infrastructure will keep Europe at the forefront of the Biological and Medical Sciences and will stimulate industrial research and commercial exploitation.

In order to prepare the creation of an efficient network of centres which provide users with optimal resources, the EU-OPENSREEN Preparatory Phase will address the following issues:

- A user-focused access strategy.
- The physical infrastructure requirements.
- Suitable data standards and the framework for a database to archive and make the results available to the scientific community.
- A financial management plan for the construction and sustainable operation of the infrastructure in cooperation with national funding bodies.
- The legal approach regarding intellectual property issues.
- An appropriate legal and governance structure.
- The development of a chemical biology education package to ensure adequate training of scientists and platform staff.
- A central chemical biology information gateway in form of a website.
- The dissemination of the business plan to stakeholders and decision makers and coordination with national funding strategies.



**1. Name and descriptive title**

**EU-OPENSREEN -  
European Infrastructure of Open Screening Platforms for  
Chemical Biology**

**2. Short description of new RI or major upgrade and main characteristics**

**“Chemical Biology”, the systematic use of chemistry to explore biology, provides unique means for unravelling complex biological processes.** Its efficacy and impact largely depends on the availability of a diverse and well-designed compound collection, the availability of modern advanced screening technologies, chemistry resources, special cell collections, and a comprehensive database and computing capacities. However, the required infrastructure exceeds the capabilities of individual institutions or even countries; therefore it is necessary to organise and implement the essential features on a large scale at the European level.

**EU-OPENSREEN is an open-access infrastructure for the development of bioactive small molecules.** It includes a large collection of diverse compounds (at least 0.5 million), high-throughput screening (HTS) centres, hit optimisation facilities, and a publicly accessible database combining screening results, assay protocols, and chemical information. The integrated infrastructure will meet the needs for new bioactive compounds in all fields of Life Sciences (human and veterinary medicine, systems biology, biotechnology, agriculture, nutrition, etc.). In the field of biomedicine, small molecules are essential for elucidating disease-relevant biological mechanisms. In this way, the infrastructure will also uncover new target classes, e.g. by exploring protein-protein interactions. In systems biology, bioactive compounds are used for perturbing complex biological networks to test mathematical models. In the areas of agriculture and nutrition, the study of metabolic pathways by means of small molecules will help to create plants with higher concentrations of desired metabolites or with a higher tolerance against diseases and other stress factors. Furthermore, small molecules may be used, for example, in biotechnology and regenerative medicine to functionalise surfaces. The European research community will benefit further from EU-OPENSREEN through activities aiming at the exchange of assay systems and cell lines, the definition of common standards, and joint training measures.

**EU-OPENSREEN brings together chemical and biological expertise** to overcome the fragmentation of European research in the field of chemical biology. Through the transnational and coordinated activities of EU-OPENSREEN a substantially accelerated generation of knowledge on the bioactivities of chemicals as well as on the responses of biological systems will be achieved. European researchers from academia will obtain access to the most advanced screening technologies that are currently only available in an industrial environment.

**The new infrastructure will stimulate industrial research** by helping to define new targets and by carrying high-risk projects one step further before they are accepted by the pharmaceutical industry. It will, furthermore, train scientists and provide invaluable data on protein-ligand interactions.

**3. Scientific Case**

**Small molecules serve as unique biochemical tools to study protein function through dosage-, time- and spatially controlled perturbations of biological systems.** It would be highly desirable to identify a specific small molecule agonist or antagonist for each function of a protein. EU-OPENSREEN thus aims at complementing the tools and technologies of molecular biology such as animal models, mutagenesis, antisense technologies, RNAi, or aptamers. However, we are currently far from adequately covering the wide variety of targets

that have emerged from genome research. Chemical biology addresses this deficit with a large-scale effort to develop new bioactive agents.

Nearly all areas of Life Sciences will profit from the availability of molecular probes in the manner described above. In **medicine**, pharmacological interventions are an essential feature of basic research since centuries. Originally, natural compounds were used, which are nowadays supplemented by synthetic compounds. Often, a variety of similar compounds is available which helps to distinguish the action of subtypes of proteins, an eminent challenge in investigations on the level of cells or organisms. The importance of small molecules in medical research is displayed, for example, in the appearance of the kinase inhibitor staurosporine in more than 2,000 research papers from the years 2000-2005. Currently, only few compounds have a similar status, but it is evident that this needs to be increased dramatically for the benefit of research in all biomedical areas.

In the context of **agriculture** and **nutrition**, novel small molecules will help in understanding metabolic pathways, with the aim to create plants containing a higher concentration of desired metabolites or which have an improved resistance against stress factors. This includes a higher tolerance against unfavourable environmental conditions such as dry habitats, especially important in view of climate change and increasing water shortages. A higher tolerance against plant diseases would be another highly desirable achievement, as the resulting reduction of herbicides, pesticides, and fungicides would benefit the farmer (lower costs), the agricultural personnel (less exposure to harmful substances), the consumer (less intake of harmful substances), and the environment.

A major goal of current Life Sciences is to obtain a systemic view of life. This implies a change of focus from single molecules to biological networks at different levels of complexity. Discovering and analysing these networks requires perturbing the activity of the involved molecular components – in most cases proteins – through genetic or chemical means, the latter corresponding to pharmacological intervention. In **systems biology** the perturbation of individual interactions or catalytic functions of a protein is an important part of the methodology, and chemical biology extends the method portfolio beyond the capabilities of knock-out techniques. It is this area, which demands for “one agonist or antagonist for each protein function”, which is intended to be satisfied by this infrastructure. In **biotechnology**, highly specific small molecules can be used for affinity purification, especially of individual protein complexes, for functionalising medically relevant surfaces, for stabilising protein preparations, for enabling crystallisation etc.. Taken together, there are many fields in current Life Sciences and even some in material sciences that will profit from a chemical biology infrastructure.

**EU-OPENSREEN will be used by researchers from universities and research institutes, who have either only limited in-house facilities or no access at all to such an infrastructure, thereby satisfying an unmet demand in the field of Life Sciences.**

EU-OPENSREEN complements the goals of other European Life Science infrastructure initiatives. One of these is **ProteomeBinders** (European Resource for Ligand Binders, <http://www.proteomebinders.org>), which aims to establish a repository of binding molecules for at least 100,000 human target proteins to provide tools for detection, quantification and characterisation of these proteins. This proteome research repository will be primarily built on antibodies and other protein receptors, but considers including small molecules as well. Thus, there will be a close interaction between EU-OPENSREEN and ProteomeBinders to exchange results and selected compounds for the ProteomeBinders repository. However, the working principles of the two infrastructures are very distinct, being on one side the screening platforms that will carry out experimental work and on the other side a repository with reagents to be distributed.

**Instruct** (Integrated Structural Biology Infrastructure for Europe, <http://www.instruct-fp7.eu/>) will maintain a set of core technologies (e.g. protein production, NMR, crystallography, different forms of microscopy), and combine this with a specific biological focus that will drive the

development of technological and methodological expertise, notably for the analysis of functional complexes. This infrastructure will be ideally complemented by EU-OPENSREEN, since small molecules may promote crystallisation and stabilise complexes, and EU-OPENSREEN will profit through the opportunity for structure-based design of small molecules.

Considering chemical biology as part of the Life Science pipeline, EU-OPENSREEN will be connected through its output – bioactive compounds – and through the required input – cell lines for assays, natural products, etc. – to initiatives providing cell or animal models like **INFRAFRONTIER** (European infrastructure for phenotyping and archiving of model mammalian genomes, <http://www.infrafrontier.eu/>), **BBMRI** (Biobanking and Biomolecular Resources Research Infrastructure, <http://www.bbMRI.eu/>), and **EMBRIC** (European Marine Biology Resource Centre <http://www.embric.eu/>). An exchange of materials and information with the two initiatives will create mutual benefits. The collaboration with various agricultural technology platforms and projects will be established through **Agri-Net** (EU-funded agricultural portal, <http://ec.europa.eu/research/agriculture/>).

The chemical biology database, a very important feature of EU-OPENSREEN, could be linked to **ELIXIR** (European Life Science Infrastructure for Biological Information, <http://www.elixir-europe.org/>) and supplement the latter's databases. In case of therapeutically relevant compounds, interactions with networks like **EATRIS** (European Advanced Translational Research Infrastructure for Medicine, <http://www.eatris.eu/>) and **ECRIN** (European Clinical Research Infrastructures Network, <http://www.ecrin.org/>) will ensure the availability of appropriate follow-up research. In particular, GLP-production of small molecules via EATRIS would be an important perspective in medically interesting cases of success.

EU-OPENSREEN is essential for European scientists to stay at the forefront of research in the Life Sciences. It will fulfil similar needs for Europe as does the **Molecular Library Program, MLP** (<http://mli.nih.gov/mli/>) of the National Institutes of Health roadmap for the USA (Austin et al. 2004 Science 32006, 1138). Both initiatives share the concept of combining screening centres, small molecule libraries, and a central database. Nevertheless both concepts are distinct in several aspects with regard to composition of chemical libraries, portfolio of services, and handling of IP issues.

#### 4. Concept Case

**The infrastructure will be composed of integrated screening platforms hosting high-throughput methodologies, a central compound management, and, as a key element, a database.** Common standards will be established for efficient transfer of materials and procedures. There will be a restricted number of screening centres with large compound collections, applying various methodologies and operating at a high degree of automation. During the Preparatory Phase the design of the infrastructure will be planned in further detail and specifications will be elaborated. Technical challenges are the creation of a large compound collection (> 0.5 million substances) and the establishment of a high degree of automation at the major sites.

The compound collection will be designed for the needs of academic screening. It should be diverse and contain well-chosen subsets for fragment-based screening, for certain protein families, or of natural products, etc. Of course, maintenance, quality control and distribution are not trivial, and appropriate procedures need to be established. The major screening centres will be highly integrated, host copies of the compound collection, and each will offer special screens corresponding to its expertise.

During the PP, a survey will be carried out in order to specify the needs of the scientific community with respect to types of screens and expertises concerning protein classes and screening technologies present at various sites in Europe. The elaboration of standards, data formats and the minimum information content of an assay constitute also important challenges.

In addition large resources are required for service chemistry to optimise hits. During the PP a survey of the various possibilities for organising hit optimisation will be performed. Of highest importance is the database which will be designed for the needs of academic screening and ligand development.

In the long run, it will become a treasure for those researchers who develop bioactive compounds, programmes for drug design etc. Further studies during the PP will include a survey of protein production facilities (existing, for example, within INSTRUCT) and of the experimental basis with respect to cell lines and animal models, including an interface to other European initiatives. These discussions will include particularly follow-up research like testing compounds on animal models, and approaches to solving ADMET- (Absorption, Distribution, Metabolism, Excretion, and Toxicity) problems.

The main elements of EU-OPENSREEN will be

- A central compound collection comprising at least 0.5 million chemical entities, including proprietary compounds, with appropriate storage and distribution systems. Focussed subsets of the collection for various biological targets will be included.
- Screening centres with high-end equipment, such as automated microscopes for cell assays or systems for automated capillary electrophoresis.
- Facilities providing efficient bio-profiling of novel natural and synthetic compounds vs. a broad variety of protein targets thus allowing rapid identification of new chemical entities (NCEs).
- Facilities for chemical optimisation of hits and development capacities for new types of assays.
- A central ADMET facility hosting appropriate cell lines and cell import systems.
- A central database combining screening results, assay protocols, and chemical information (European Chemical Biology Database, ECBD). The database could be linked to existing genomic and proteomic databases through ELIXIR (<http://www.elixir-europe.org/>), the European Life Science Infrastructure for Biological Information, an initiative coordinated by the European Bioinformatics Institute (EBI).
- An efficient and speedy evaluation of incoming applications will be organised by the central management office, involving both external and internal experts in the field of chemical biology.

It is envisaged to create a legal entity, such as e.g. a European Research Infrastructure Consortium (ERIC), in order to facilitate the interaction of the stakeholders involved and their cooperation with the external users. EU-OPENSREEN membership will be open to all European organisations involved in chemical biology and willing to offer access to external scientists. A central research and training facility will be established, including a central management office.

**Rules for the handling of Intellectual Property (IP) related issues have to be defined.** The general approach will be to set up a flexible framework for IP issues in order to allow for a protection of knowledge before including the results in the database.

EU-OPENSREEN's mission to create an open platform for the enhancement of the exploitation of chemical entities for studying biological processes is not encouraged by patent law, since a lack of affordable early options for IP protection inhibits disclosure of research discoveries and their deposition in an open database. EU-OPENSREEN will stimulate and support activities towards advancement of the current patenting situation. Activities should particularly address the needs of large data repositories and open collaborative networks,

which require a balance between rapid knowledge sharing on the one hand and protection and exploitation activities on the other hand.

The establishment of EU-OPENSREEN requires a **3 years Preparatory Phase**. The costs for operation include finances for maintaining the compound library, for addition of new compounds, for maintenance of the HTS machinery, and for development of novel screening technologies, plus personnel costs. A total of 40 Mio € as initial investments for the various sites and the central facility will be required and running costs per year in the range of 40 Mio €, including personnel and consumables.

#### **5. Further information, including strategic importance to ERA**

A key element of EU-OPENSREEN will be a common database (European Chemical Biology Database, ECBDB), where all data generated are collected and made available to the public. It will be linked to existing genomic and proteomic databases through ELIXIR, the European Life Science Infrastructure for Biological Information (<http://www.elixir-europe.org/>), an initiative coordinated by the European Bioinformatics Institute (EBI). Links to DRIVER (Digital Repository Infrastructure for European Research, <http://www.driver-repository.eu/>) could be established as well. The European Chemical Biology Database established within EU-OPENSREEN will become an extremely valuable treasure for e.g. biotechnology, agriculture and future drug development in Europe.

#### **6. Identification of other socio-economic impacts**

**The broad interdisciplinary chemical biology approach of EU-OPENSREEN (covering all areas of molecular Life Sciences) brings together chemists, engineers, informaticians and biologists and creates numerous opportunities for innovation and commerce.** Bioactive chemical compounds are not only the most common form of medical therapies, they are also of great relevance for agriculture, nutrition and biotechnology. Thus EU-OPENSREEN opens new paths for research in the post-genomic era and its most direct translation from basic science into improved quality of life. All Life-Science-based activities will therefore profit from EU-OPENSREEN. In particular, EU-OPENSREEN will focus on high-risk research, which precedes commercial development of innovative bioactive compounds. **Unlike commercial screening platforms and pharmaceutical industry, it will mainly use non-validated targets and identify entire new target classes, which will dramatically broaden the basis for the commercial developments of bioactive compounds.** In addition, the infrastructure will establish a comprehensive database, which exceeds by far the information provided by commercial screening platforms and therefore represents an entirely new resource, currently not available to European researchers. Thus, the new infrastructure will not compete with commercial screening platforms, whose focus is on drug development, using mainly validated targets. On the contrary, it will feed the development pipelines of the European industry. It will promote competitiveness, growth and jobs, economic and social cohesion: all essential components of the overarching objective of sustainable development, as laid out in the Lisbon Agenda. The initiative is firmly supported by various European companies.

**For the first time, the distributed infrastructure will offer European researchers from academia access to the most advanced screening technology that is currently only available in pharmaceutical industry** and which underlies many restrictions (e.g. financial restrictions and restrictions regarding IP). In addition, the interdisciplinary research will lead to novel screening technologies and supporting test systems which are initially only available in the academic environment. Moreover, it will to a great extent bioprofile proprietary compounds provided by chemists from Europe. Finally, the inherent training aspect is intensified through the establishment of links between universities and research institutes on the one hand and SMEs and large companies on the other hand. Thus, EU-OPENSREEN activities exceed by far those of commercially available screening services.



**The initiative will contribute to better protection and improvement of health, have an impact on farming and food production, and therewith encourages and facilitates innovation, research, and development in pharmaceutical, biotechnology, healthcare and agricultural areas.**

The research-based biopharmaceutical, food and agricultural industry is of great importance for European citizens as well as for the economic future of Europe. However, the number of NCEs reaching the market has been decreasing in the past years, whereas industrial investment in R&D has been constantly increasing.

EU-OPENSREEN will target these challenges because it will

- elucidate the underlying mechanisms of complex biological pathways and therewith boost scientific research and development in the all fields of Life Sciences, and
- broaden the basis for the commercial development of bioactive compounds,
- bridge the gap between academic research projects and the commercial development of bioactive compounds,
- secure IP from academic projects for commercialisation,
- promote the availability of safe and efficacious chemical products for so far unmet needs in medicine, nutrition and agriculture.

EU-OPENSREEN will thus assure that the scientific treasures of European research in the field of Chemical Biology are optimally exploited for the benefits of research and society.

#### ***7. Commitments/maturity: Which states/organisations have demonstrated interest/commitment in supporting and/or funding the proposal?***

In recent years the need for a coordinated chemical biology approach already lead to the development of several regional initiatives e.g. in France, Germany, Scandinavia, Spain and the United Kingdom. In several further countries such as Austria, the Czech Republic, Israel, Italy, Poland, and Switzerland institutes with chemical biology expertise have evolved. However, the capacities of these emerging, local screening platforms are far from being able to meet the demand in a European context.

**EU-OPENSREEN will overcome these limitations** by setting up an integrated infrastructure for interdisciplinary chemical biology projects in Europe. Thereby it will provide a central resource for discoveries and innovation in chemical biology and related fields.

**Stakeholders from all countries listed below have declared their commitment to EU-OPENSREEN. Further organisations or countries may want to become involved. This will be explored before and during the Preparatory Phase following defined extension criteria.**

- **Austria:** Research Center for Molecular Medicine of the Austrian Academy of Sciences (CeMM) (<http://www.cemm.at>). The scientific director, Prof. Giulio Superti-Furga, is dedicated to „integrative systems biology“ and wants to use small molecules for pull-down of protein complexes. He supports strongly the establishment of an Austrian platform for chemical biology (PLACEBO, PLatform Austria for ChEmical BiOlogy).
- **France:** Several regional and national screening initiatives have been started since 2003. The French Screening Network includes centres in Strasbourg, Saclay, Roscoff, Toulouse, and Grenoble. In addition, Centre National de la Recherche Scientifique (CNRS) and others have established a French National Chemical Library (<http://chimiotheque-nationale.enscm.fr/>) which would be a major asset of the EU-OPENSREEN consortium.
- **Germany:** The ChemBioNet, a Resource Network to Support Chemical Biology

Research in Academia (<http://www.chembionet.info/>), offers HTS services since 2004; founding institutes are “Leibniz-Institut für Molekulare Pharmakologie” (FMP), Berlin, “Helmholtz-Zentrum für Infektionsforschung” (HZI), Braunschweig and “Max-Delbrück Centrum für Molekulare Medizin” (MDC), Berlin; the central screening platform and the compound collections are located at FMP Berlin.

- **Czech Republic:** The Institute of Molecular Genetics (IMG), Prague (<http://www.img.cas.cz/>) has numerous groups working on proteins with chemical biology methods including phenotypic screening assays. A Czech Chemical Biology Initiative (CCBI, <http://www.chembio.cz/>) has formed.
- **Norway and Sweden:** The Scandinavian Chemical Biology Platform maintained by both countries covers all aspects of chemical biology; key players are University of Oslo (Prof. Kjetil Taskén, [http://www.biotek.uio.no/research/tasken\\_group/](http://www.biotek.uio.no/research/tasken_group/)) and Umeå University (Profs. Mikael Elofsson, F. Almkvist, A. Linusson, <http://www.chemistry.umu.se/forskning/group-leaders/mikael-elifsson>). A Swedish Chemical Biology Consortium has formed with Umeå University, Uppsala University and Karolinska Institute as three coordinated nodes which is funded by the Swedish Research Council and participates in EU-OPENSREEN.
- **Denmark:** The Technical University of Denmark (DTU, <http://www.dtu.dk/English.aspx>) is the hub for the chemical biology research in Denmark. Professor Thomas E. Nielsen of DTU is a founder of the Danish Chemical Biology Initiative (DCBI; web-site will soon be launched at: [www.chemicalbiology.dk](http://www.chemicalbiology.dk))
- **Finland:** The Institute for Molecular Medicine Finland (FIMM, <http://www.fimm.fi/en/>) of the University of Helsinki (director: Olli Kallioniemi) is a member of the EMBL Molecular Medicine Partnership and the site for the major national infrastructure with open access to both academia and companies. Krister Wennerberg directs this major HTS facility.
- **Israel:** Prof. Alexander Levitzki, the Hebrew University of Jerusalem (<http://biolchem.huji.ac.il/levitzki/levitzki.html>), is an outstanding protagonist of chemical biology, representing the community from Israel. He is an expert in the development of kinase inhibitors with a long track record in industrial applications.
- **Italy:** The CISI - Centre of biomolecular Interdisciplinary Studies and Industrial Applications - is located at the University of Milan (<http://users.unimi.it/dpcorind/en/>). Headed by Prof. Carlo Scolastico the centre offers expertise on high throughput synthesis, combinatorial chemistry, molecular modelling and chemical analysis for chemical biology projects.
- **Netherlands:** Based on the renowned screening experience of the Netherlands Cancer Institute (NKI, <http://www.nki.nl/>) and the Dutch chemical expertise, Prof. Herman Overkleeft (Univ. Leiden) and Huib Ovaa (NKI) are establishing the Dutch Compound Library (DCL) and the “Netherlands Open Screening Network”.
- **Poland:** Contacts to the polish community are established through Dr. Zbigniew Lesnikowski of the Institute for Medical Biology – Polish Academy of Sciences. Prof. Piotr Zielenkiewicz, who is director of the Institute of Biochemistry & Biophysics, Polish Academy of Sciences, and heads the Department of Bioinformatics (<http://www.ibb.waw.pl/staff/bioinf.html>). He is interested in the modelling of metabolic pathways and molecular crowding, adding a systems biology component.
- **Spain:** The Spanish Drug Discovery Platform (<http://www.pcb.ub.es/drugdiscovery>) is supported by groups in the Barcelona Science Park, the screening platform at Santiago de Compostela (<http://www.usc.es/>) and other groups in Spain. It includes a national compound collection, the Spanish ChemBioBank, located in Barcelona.
- **Switzerland:** The Swiss community is represented by the École polytechnique fédérale de Lausanne (EPFL) (<http://bsf.epfl.ch/>) screening facility which covers all important aspects for the development of bioactive compounds. It is headed by Dr. Gerardo Turcatti who has valuable industrial experience in drug development.

- **United Kingdom:** Chemical biology in the UK is strongly supported by the Wellcome Trust which has established several major screening facilities. Dr. Julie Frearson, University of Dundee (<http://www.lifesci.dundee.ac.uk/>), is head of probably the largest screening unit focusing on tropical diseases and represents this community. In Cambridge small molecule screening has been linked to protein crystallisation (<http://www.bioc.cam.ac.uk/uto/blundell.html>).
- **European Bioinformatics Institute (EMBL-EBI):** EMBL-EBI provides freely available data and bioinformatics services to all facets of the scientific community and contributes to the advancement of biology through basic investigator-driven research in bioinformatics, also by helping to disseminate cutting-edge technologies to industry. The EMBL-EBI will coordinate the creation of the central data infrastructure for EU-OPENSREEN, guide the design and implementation of the data analysis software and lead the work on standardisation.

**An important feature of the proposed infrastructure is that it is open to further interested parties and emerging screening centres.** Partners in the Preparatory Phase are listed in the following Table 15:

**Table 15:** Preparatory Phase partners of EU-Openscreen

Participant no.	Participant organisation name	Country
FMP	Forschungsverbund Berlin e.V. (FVB) – Leibniz-Institut für Molekulare Pharmakologie	DE
HZI	Helmholtz-Zentrum für Infektionsforschung GmbH	DE
UiO	Universitet i Oslo	NO
PCB	Fundacio Privada Parc Cientific de Barcelona	ES
UmU	Umeå Universitet	SE
IMG	Institute of Molecular Genetics AS CR	CZ
EMBL-EBI	European Molecular Biology Laboratory – Outstation European Bioinformatics Institute	INO
FIMM	Institute for Molecular Medicine Finland	FI
CeMM	Centre for Molecular Medicine	AT
DTU	Danmarks Tekniske Universitet	DK
IMB	Institute for Medical Biology – Polish Academy of Sciences	PL
NKI	Netherlands Cancer Institute	NL
CNRS	Centre National de la Recherche Scientifique	FR
BMBF	Bundesministerium für Bildung und Forschung	DE
WGL	Wissenschaftsgemeinschaft Gottfried Wilhelm Leibniz e.V.	DE
HGF	Helmholtz-Gemeinschaft Deutscher Forschungszentren e.V.	DE
CISI SCRL	Consorzio Interdisciplinare Studi bio-molecolari ed applicazioni Industriali, SCRL	IT

Several organisations have expressed their interest in EU-OPENSREEN and have provided Letters of Support.



Governmental organisations and funding agencies

BMBF – Bundesministerium für Bildung und Forschung, Germany  
 WGL – Wissenschaftsgemeinschaft Gottfried Wilhelm Leibniz e.V., Germany  
 HGF – Helmholtz-Gemeinschaft Deutscher Forschungszentren e.V., Germany  
 Senatsverwaltung für Bildung, Wissenschaft und Forschung, Berlin, Germany  
 MICINN – Ministerio de Ciencia e Innovación, Spain  
 RCN – Research Council of Norway  
 BMWF – Federal Ministry of Science and Research, Austria  
 Ministère de l'Enseignement Supérieur et de la Recherche, France  
 CNRS – Institute of Biological Sciences, France  
 CNRS – Chemistry Institute, France  
 Swedish Research Council  
 Swedish Foundation for Strategic Research  
 Polish Ministry of Science and Higher Education  
 Finnish Ministry of Education  
 NWO – Netherlands Organisation for Scientific Research

Other stakeholders

SwedenBio  
 EATRIS – European Advanced Translational Research Infrastructure in Medicine  
 EMBRC – European Marine Biological Resource  
 Euro-Biolmaging – European Biomedical Imaging Infrastructure  
 E-Rare – ERA-Net for research programmes on rare diseases  
 Joint Chemical Biology Division (DECHEMA, GDCh, GBM, DPhG), Germany  
 ESP – European ScreeningPort, Germany  
 AstraZeneca, Sweden  
 Bayer Schering Pharma, Germany  
 QCL – Queensland Compound Library, Australia  
 Eskitis Institute of Cell and Molecular Therapies, Australia

**8. Costs for construction, operation and decommissioning, indications on project financing.**

Preparatory cost	Construction cost	Operation cost (total)	Decommissioning cost
3.7 Mio €	40 Mio €  to be further determined in the Preparatory Phase	approx. 40 Mio €/year  to be further determined in the Preparatory Phase	Not applicable

**9. Timetable for construction, operation and decommissioning with duration and possible starting dates.**

Preparatory phase	Construction phase	Operation	Decommissioning
3 years	1.0 year	>10 years	-

**10. Reference: Person who has submitted the proposal and will follow up in ESFRI.**

Dr. Ronald Frank  
 Leibniz-Institut für Molekulare Pharmakologie (FMP) im Forschungsverbund Berlin e.V.  
 Robert-Rössle-Str. 10  
 13125 Berlin  
 Germany  
 Phone: +49-(0)531-61813400  
 Fax: +49-(0)30-94793109  
 Email: [info@eu-openscreen.eu](mailto:info@eu-openscreen.eu)  
<http://www.eu-openscreen.eu>

**11. Progress in the Preparatory Phase**

The EU-OPENSREEN Preparatory Phase initiative will start on the 1<sup>st</sup> November, 2010. The objectives will be to elaborate and reach consensus between the organisations involved (ministries, funding bodies and scientific institutions) on a detailed plan for the construction and operation of a European infrastructure of open-access technology platforms for chemical biology (see Figure 28).

Legal, Governance and Logistical work:

A legal structure will be chosen that suits a distributed, pan-European Research Infrastructure with partners from different countries (e.g. the new ERIC). A legal framework will be developed to address all prerequisite legal issues such as the types of contracts used for cooperations between institutions and users (WP6). The governance structure of EU-OPENSREEN will also be developed in this WP to ensure that the two structures are compatible. The governance structure has to support efficient decision-making, enable the extension of EU-OPENSREEN, ensure efficient coordination of strategic activities with other ESFRI BMS infrastructures and support effective day-to-day management. EU-OPENSREEN's involvement with potential drug and target candidates affords careful consideration of intellectual property rights and suitable regulations and agreements will be established (WP8). In order to keep all relevant parties informed about the EU-OPENSREEN activities and to coordinate this Research Infrastructure with other European initiatives (e.g. EATRIS, EMBRC, EuroBioImaging, BBMRI, ELIXIR), a website will be created as a central information gateway. Coordination with other ESFRI BMS infrastructure initiatives will secure public visibility and contribute to the effective integration into the European Research Area (WP4).

Strategic work:

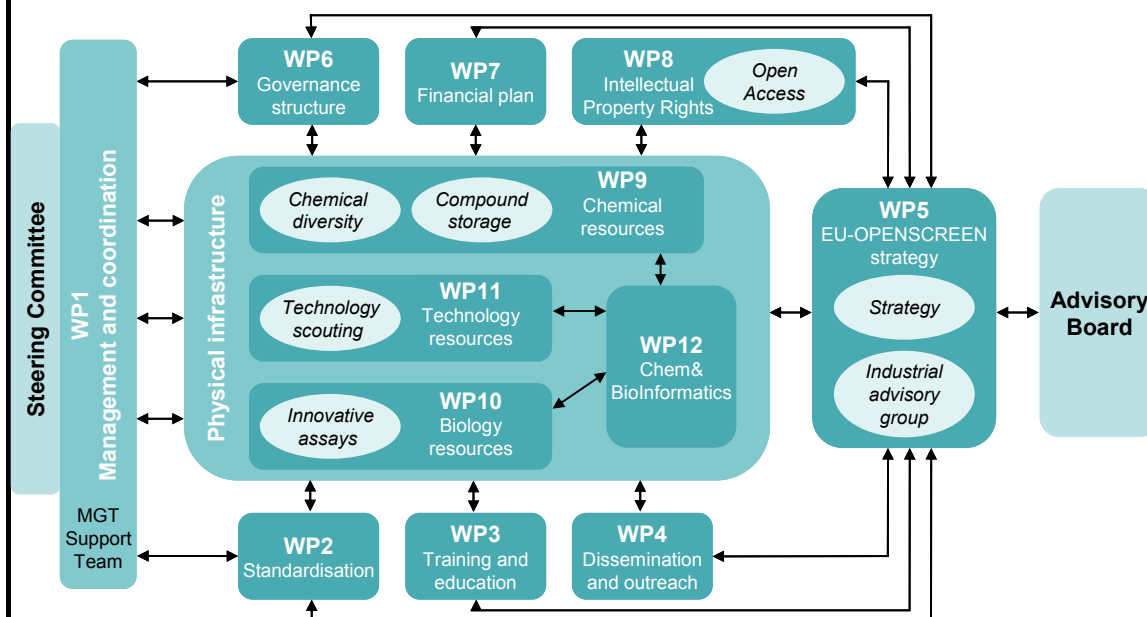
A user strategy and minimum standards for EU-OPENSREEN centres will be defined in order to provide users with appropriate access to high quality facilities. This will involve stakeholder meetings, national and global surveys (WP5) as well as non-supported activities in the various EU Member States to coordinate national consortia (WP13). Suitable concepts for training and education in the interdisciplinary field of chemical biology will be developed in order to educate staff and future generations of scientists (WP3).

Financial work:

Implementation of EU-OPENSREEN will be based on a consortium of existing centres whose operations are supported by the parent institutes. A financial concept and management plan will be established (WP7) that includes financial controlling mechanisms as well as a business plan for the implementation and sustainable operation of a distributed pan-European infrastructure. Surveys on costs for capacity upgrades to existing facilities, for construction of new facilities and for operation with transnational access will be conducted, as well as an evaluation of investment models and funding options. Additional sources such as structural funds and other sponsors will also be recruited.

**Technical work:**

The detailed technical refinement of the infrastructure facilities needed to match the EU-OPENSOURCE user concept will be conducted (WP9-11). Common standards for exchange and deposition of data will be established (WP2), which will lead into the development of the ECBD and mechanisms for how it will be linked to other European databases such as ELIXIR and DRIVER (WP12).

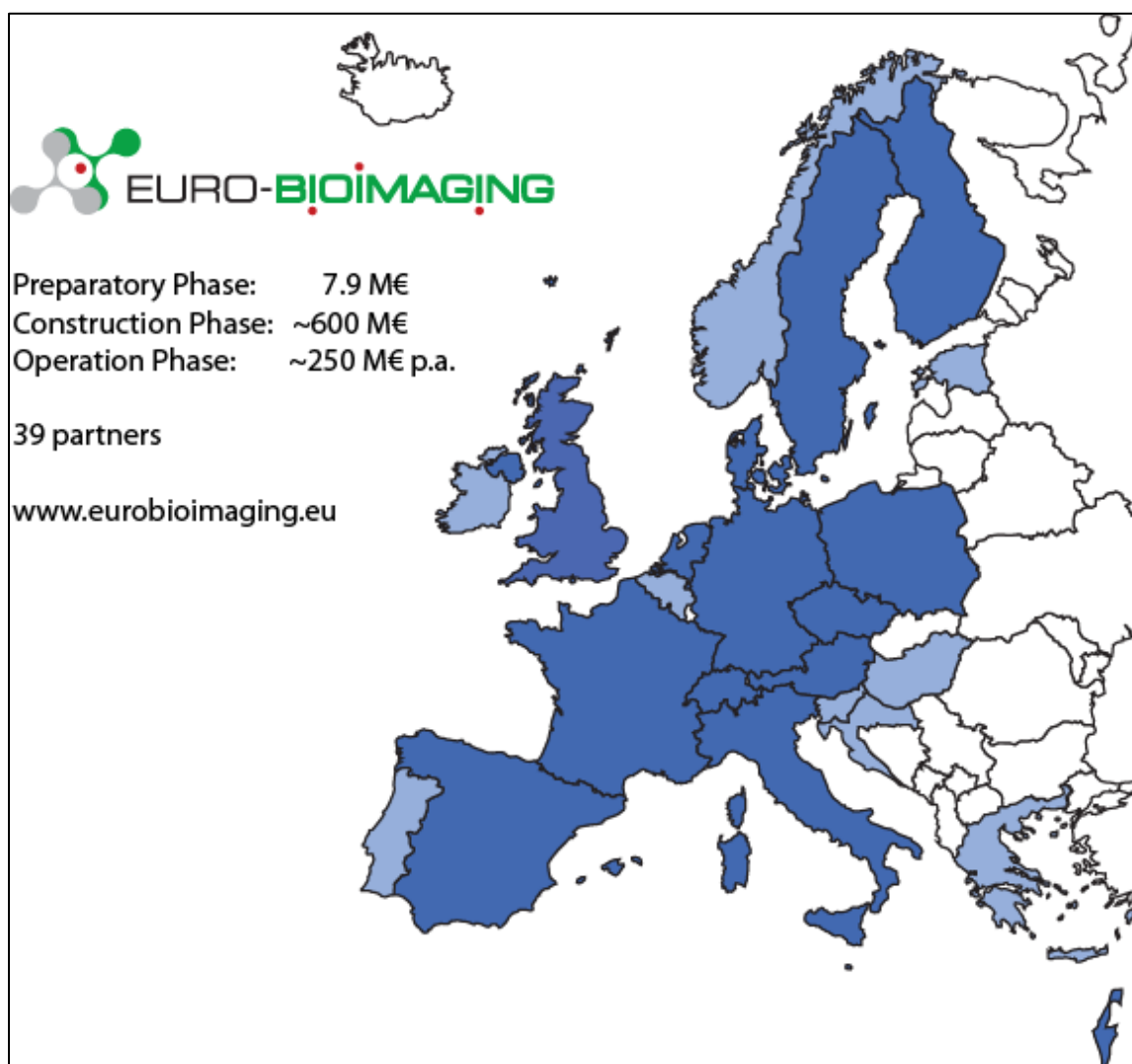


**Figure 28:** Plan for the construction and operation of a European infrastructure of open-access technology platforms for chemical biology

**Table 16:** Links between Research Infrastructures – EU-OPENSOURCE

	EU-OPENSOURCE	Further specification of the technological link	Further specification of the thematic link	Short statement for further specification (last update February 2010)
BBMRI		Small molecule additions to inventory of specific ligands for human proteins (ProteinBinders)	Validated research reagents and diagnostic tools for the detection of protein targets in biological samples	
EATRIS		Bioactive compounds from the EU-OPENSOURCE repertoires will be processed to drug candidates and leads by EATRIS. On the other hand, specific assay development and verification of drug candidates / leads could be performed	Open innovation in the field of medical drug development by joint efforts in the identification and development of bioactive small molecules for clinical applications.	
ECRIN		Only indirect! Post-EATRIS clinical investigation of drug leads	Medical drug development	
ELIXIR		e-Infrastructure and database for linking biomolecular and chemical-biology data	Support chemical biology data exchange and public domain open access drug-discovery	
Infrafrontier		Bioactive compounds and drug leads for <i>in vivo</i> testing; <i>in vivo</i> mode of action	Proof of concept for <i>in vivo</i> activities of biologically active compounds	Bioassays of compounds from EU-OPENSOURCE test pipelines in Infrafrontier mouse clinics
INSTRUCT		Small molecules for analysis with protein structure	Mechanism of action of small molecules at atomic resolution; Drug design	
EMBRIC		Testing and provision of novel marine secondary metabolites for bio-medicine and life sciences	New chemical diversity from biodiversity	
ERINHA		ERINHA will be the European structure where antimicrobial drugs efficacy can be tested on living risk group 4 pathogen. This include those identified through prescreening by EU-openscreen. Some screening test that requires BSL4 containment could be done through	Discovery and validation of new anti-infective compounds	
Euro-BioImaging		Image capture and analysis of morphological or reporter signals in cell-based screening assays (high-content screening) is becoming an important alternative to single target <i>in vitro</i> screening	Image-based high-content screening and drug profiling	Euro-BioImaging plans a combined infrastructure for high throughput microscopy and chemical screening facility
e-IRG				
SSH				
ESP				
ENV				
ENE				

#### 4.6.4 Research Infrastructure for Imaging Technologies in Biological and Biomedical Sciences (Euro-BiolMaging)



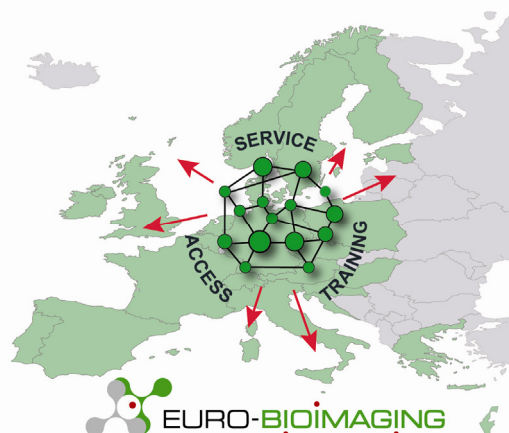
Research in and application of, bio-molecular and biomedical imaging is progressing rapidly and increasingly this growth is in a multidisciplinary manner. Innovative imaging techniques are key tools for all life scientists to understand living systems at both the molecular and the physiological level, from biological model systems to patients.

Euro-BiolMaging aims to become a European Research Infrastructure for biomedical imaging stretching from basic biological imaging with advanced light microscopy up to the clinical and

epidemiological level of medical imaging of humans and populations.

Euro-BiolMaging will consist of a number of widely distributed and strongly coordinated biomedical imaging infrastructure facilities, which will serve European scientists by providing access to and training in advanced imaging technologies across the full scale of biological and medical applications. At the same time the infrastructure will provide the possibility for many existing imaging research institutions or laboratories to contribute to knowledge development and training. Euro-BiolMaging will also serve as a platform delivering knowledge and

expertise, allowing exchange of methodologies and the joint use of acquired data (see Figure 29).



**Figure 29:** Key deliverables of Euro-BioImaging

Once being established Euro-BioImaging will impact academic research and greatly accelerate the accessibility of imaging methods, will further advance research in new and emerging imaging technologies and support members of the European Union in staying at the cutting edge development of state of the art techniques. Societal impact will be increased by fostering collaboration between all stakeholders including industry, regional, national and European authorities, and multidisciplinary scientists involved in the field of imaging research. The liaison with public and private sponsors will foster the establishment of strategic priorities and areas for possible cooperation.

Euro-BioImaging seamlessly fits in the European and global Research Infrastructure landscape and will closely collaborate with other ESFRI Research Infrastructures in the Biomedical Sciences as well as e-Infrastructures. Given the cross cutting nature of imaging technologies, Euro-BioImaging expects to provide expertise in and access to innovative imaging technologies to virtually all BMS Research Infrastructures.

The start of the Preparatory Phase is envisaged for December 2010. The Preparatory Phase consortium comprises a set of 39 beneficiaries from 15 ESFRI Member States. These core partners represent leading scientists in the different imaging technologies and infrastructures as well as key political and funding bodies. In addition, Euro-BioImaging has already assembled a valuable set of more than 80 associated partners representing 23 ESFRI Member States. Furthermore, the strong interest in this infrastructure project has been expressed by 125 universities, research councils, ministries, funding organisations and industry.

In order to ensure a comprehensive consultation and engagement process from the beginning and to build a community of international stakeholders Euro-BioImaging conducted its first stakeholder meeting in September 2009. More than 250 participants from 24 countries attended the key note lectures and actively contributed in ten work package specific breakout sessions. A second stakeholder meeting will take place in October 2010.

### 1. Name and descriptive title

## Euro-Biolmaging - Research Infrastructure for Imaging Technologies in Biological and Biomedical Sciences

### 2. Short description of new RI or major upgrade and main characteristics

Imaging technologies are core disciplines of tomorrow's biology and medicine, and represent essential new Research Infrastructure for the Life Sciences. Now is the time to provide broad access to state of the art and new emerging imaging technologies to the European scientific community, to strengthen research and training in imaging and to ensure European leadership in this competitive field.

Euro-Biolmaging ([www.eurobioimaging.eu](http://www.eurobioimaging.eu)) brings together key research areas in imaging technologies stretching from basic biological imaging with advanced light microscopy (ALM), *in vivo* molecular imaging of single cells to animal models up to the clinical and epidemiological level of medical imaging of humans and populations. With this broad vision of imaging, Euro-Biolmaging will address the imaging requirements of both biological and medical imaging research communities by creating a coordinated and harmonised plan for infrastructure deployment in Europe.

Euro-Biolmaging infrastructures will provide access to state of the art equipment across the full spectrum of biological and medical applications as well as to provide training and continue the development of imaging technologies to be able to offer them as new services. The vision of Euro-Biolmaging is to provide a clear path of access to imaging technologies for every biomedical scientist in Europe.

The Euro-Biolmaging infrastructure will be focused on complementary imaging technologies and address different aspects of biology, physiology and pathophysiology and develop a plan to construct and operate a distributed set of complementary infrastructure facilities, to allow focused use of resources.

Euro-Biolmaging will create a widely distributed and strongly coordinated infrastructure for biomedical imaging in Europe. ("hub-and-node" model). Euro-Biolmaging will serve European scientists by providing access to advanced imaging technologies and at the same time provide the possibility for many existing imaging research institutions or laboratories to contribute to knowledge development and training. In addition, Euro-Biolmaging will create a coordination platform delivering knowledge and expertise, allowing exchange of methodologies and the joint use of acquired data.

### 3. Scientific Case

Euro-Biolmaging infrastructures will meet the challenge for access to state of the art equipment as well as provide training and continue the development of imaging technologies. As imaging methods are grouped around different scales of biological organisation, from the molecule to the human organism, Euro-Biolmaging imaging infrastructure will be complementary, rather than redundant, to allow focused use of resources in dedicated centres of excellence. The over-arching Euro-Biolmaging goal is to provide Research Infrastructures for multidisciplinary projects by combining biologists, chemists, physicists, bioengineers, computer scientists, imaging technologists and clinicians in order to deliver world class methods for biological and medical applications.

It will be vitally important to integrate Euro-Biolmaging into the European and global Research Infrastructure landscape. The first step towards this goal will also be intimate collaborations



with other ESFRI Research Infrastructures in the Biomedical Sciences as well as e-infrastructures. In fact given the cross cutting nature of imaging technologies, Euro-Biolmaging expects to provide expertise in and access to innovative imaging technologies to virtually all BMS RIs.

Together with **ECRIN** ([www.ecrin.org](http://www.ecrin.org)) Euro-Biolmaging will work on the establishment of new quality standards for clinical trials for imaging technologies and clinical trials using imaging biomarkers at the European level. **EATRIS** ([www.eatris.eu](http://www.eatris.eu)) has several sites where imaging is an integral activity. Euro-Biolmaging will provide EATRIS with access to imaging services and standards for methods, data, and user training. Euro-Biolmaging will collaborate with **INFRAFRONTIER** ([www.infrafrontier.eu](http://www.infrafrontier.eu)) by offering services in developing imaging methods for mouse models, e.g. by establishing common imaging programmes. In discussion with Euro-Biolmaging, **INSTRUCT** ([www.instruct-fp7.eu](http://www.instruct-fp7.eu)) already expressed specific interest to develop a common infrastructure for correlative light and electron microscopy. Euro-Biolmaging will seek collaboration with **BBMRI** ([www.bbmri.eu](http://www.bbmri.eu)), the key resource for the development of biomarkers, by providing innovative image analysis tools. Together with **EMBRIC** ([www.embric.eu](http://www.embric.eu)), Euro-Biolmaging will evaluate marine organism models for imaging and Euro-Biolmaging will provide imaging facilities for marine organisms. Euro-Biolmaging plans to evaluate deployment of an imaging infrastructure into high security laboratories in collaboration with **ERINHA** ([www.hbsl.eu](http://www.hbsl.eu)) and a joint survey of pathogen and imaging communities will be conducted. Together with **EU-OPENSOURCE** ([www.eu-openscreen.de](http://www.eu-openscreen.de)), Euro-Biolmaging plans a combined infrastructure for high-throughput microscopy and chemical screening facility. A common infrastructure for image databases and public repositories could be set up within **ELIXIR** ([www.elixir-europe.org](http://www.elixir-europe.org)) to avoid duplicated efforts and profit from synergies.

Euro-Biolmaging will also be linked to the existing large scale physics facilities such as ultra-high field magnetic resonance systems becoming available within NEUROSPIN to integrate new ideas for the development of novel, innovative imaging procedures.

Euro-Biolmaging will closely collaborate with the European Light Microscopy Initiative (ELMI, [www.embl.org/elmi](http://www.embl.org/elmi)) and the European Institute for Biomedical Imaging Research (EIBIR, <http://www.eibir.org/>). ELMI comprises a wide network of European advanced light microscopy facilities in almost each ESFRI Member State. EIBIR has the aim of coordinating and supporting the development of biomedical imaging technologies and the dissemination of knowledge with the ultimate goal of improving diagnosis, treatment and prevention of disease. ELMI and EIBIR already organize training courses and conferences in advanced light microscopy and medical imaging.

Particular attention will also be devoted to integrate the activities of Euro-Biolmaging with the major European scientific associations and research initiatives in the field. Examples are projects such as European Network for Cell Imaging and Tracking Expertise (ENCITE), quantitative imaging data in human cells by automated microscopy (MITOSYS). There are also a number of "Network of Excellence" consortia currently funded by the European Commission, which could interact strongly with the proposed infrastructure.

#### 4. Concept Case

Euro-Biolmaging infrastructure will cover imaging technologies ranging from general advanced light microscopy, innovative ALM technologies, via molecular imaging to innovative medical imaging technologies up to patient and population imaging. It will be newly constructed or undergo major upgrades in order to devote a significant part of their capacity to external users. In this manner, the infrastructures will provide access to imaging technologies across the full scale of biological and medical applications in an integrated manner, allowing translation of new developments from laboratory to clinical use.



Strongly interlinked distributed infrastructure facilities will set the pan-European foundation for Euro-BiolMaging and will offer access to training in:

- a broad range of fluorescence microscopy methods
- innovative imaging technologies which are not easily accessible, still under development, or not yet commercially available
- optical tomography and related light microscopy methods as well as multi-modal molecular imaging in animal models and the development and testing of new imaging probes
- standardised infrastructures for clinical trials in imaging, image guided interventions and population based imaging
- quantitative image processing methods, database models and data storage tools

In the Preparatory Phase a plan to construct and operate the Euro-BiolMaging infrastructure will be developed and additional topics will be evaluated based on the needs of the community. Thus, new and emerging areas that are becoming increasingly relevant for biomedical imaging may be included in the Euro-BiolMaging infrastructure.

The strategic objectives of the initial phase of Euro-BiolMaging are to define the legal, governance and financial framework under which the infrastructure will be constructed and operated and to develop an overarching business plan that provides the realistic basis for construction of the Euro-BiolMaging infrastructure.

Through the combination of these technical and strategic objectives, Euro-BiolMaging will be able to address the key elements of successful infrastructures: supporting research, training and innovation. Societal impact will be increased by fostering collaboration between all stakeholders including industry, regional, national and European authorities, and multidisciplinary scientists involved in the field of imaging research.

### **5. Further information, including strategic importance to ERA**

E-infrastructure is an integral part of the Euro-BiolMaging proposal and it will make extensive use of the existing e-infrastructures in Europe (GÉANT, PRACE). With the increasing automation of ever more complex experimental protocols, the amount of digital image data that is currently generated is growing exponentially. Single high-throughput or high-resolution imaging experiments can, for example, generate data volumes of multiple terabytes. This will place substantial demands on data storage infrastructure, but even more importantly requires Euro-BiolMaging to make the tools available to process digital image data using high performance computing. Euro-BiolMaging will be linked to e-infrastructures and high speed data network initiatives and already envisions launching a joint project with INFRAFRONTIER to develop a pilot project for the interaction with the e-infrastructures.

Furthermore, driven by the power of computerised image processing the data produced will be quantitative rather than qualitative to enable systems biology and imaging biomarkers. This means that comparison of data sets, and centralised repositories for rapid and machine readable retrieval, are a key emerging need in the imaging community. On one side this will be solved by a common infrastructure within the ELIXIR RI. On the other side connecting large image databases with clinical and genetic information and developing intelligent data-mining algorithms will allow the extraction and establishment of new relations between genotypes and imaging phenotypes.

## **6. Identification of other socio-economic impacts**

Biomedical imaging is the central technology platform of both biomedical research and health care practice. The field is currently booming with innovation and Europe has a leadership position with many of the large and medium-sized industries based in Europe. Improved health care for European citizens will translate into economic advantages for the society, and the discovery of new products, new equipments, and new diagnostic and therapeutic procedures will represent important income for the institutions involved. As the health care market is growing fast the activities carried out within Euro-Biolmaging are expected to yield a marked increase of the European IP in fields ranging from imaging methods to innovative diagnostic methods.

Euro-Biolmaging will be equipped with the most advanced instrumentation for a wide range of imaging modalities and it will be endowed with the capability of developing suitable molecular probes as well as the proper cellular and animal models to study a given pathology. Once techniques have been developed, anything visualised at a molecular/cellular level could be used in a therapeutic approach, to help diagnosis, guide therapy and design drugs. Once better resolution and enhanced image processing is available, imaging modes across different scales of biological organisation will become quantitative, a key prerequisite for systems biology and the development of imaging biomarkers.

Euro-Biolmaging will also establish strong ties with European industry. Traditionally, European industry has held a worldwide leadership in the field of imaging technologies (Carl Zeiss (DE), Leica Microsystems (DE), Olympus (DE), Philips (NL), Siemens (DE), Bayer-Schering (DE), GE Health Care (UK), Bracco (IT), Guerbet (FR)). Several of these leading companies have already expressed their interest in the Euro-Biolmaging infrastructure and may actively contribute to the development of technology and biological applications at Euro-Biolmaging, where a multidisciplinary environment and cutting edge research applications will be readily available. This will allow industry partners to define new concepts faster and deliver prototypes closer to the final product, significantly increasing their competitiveness and generating added European value.

Euro-Biolmaging will have a major impact on the skills of European scientists by addressing the common needs for training in advanced state of the art imaging instrumentation for Life Science research in many ESFRI countries. Training will be performed at the Euro-Biolmaging infrastructure for the specific biomedical imaging technologies. This training will cover all aspects necessary to obtain conclusive data using the technology, ranging from specimen preparation to data collection and analysis. This will disseminate expert skills in the scientific community and ensure maximum return in the use of the advanced technologies.

Euro-Biolmaging will therefore support members of the European Union in staying at the cutting edge development of state of the art biomedical imaging techniques and serve as a platform of excellence for European scientists working in pertinent fields of biomedical imaging and catalyse scientific exchange and collaboration.

Euro-Biolmaging will consider itself a success once every research institution or research activity in Europe would have access to and training in the imaging technologies they need through defined access models and training curricula as well as effectively disseminated information concerning what imaging technologies and infrastructure exist where, and by so doing, improve European competitiveness in biomedical imaging.

**7. Commitments/maturity: Which states/organisations have demonstrated interest/commitment in supporting and/or funding the proposal?**

Euro-Biolmaging is headed by two scientific coordinators, Jan Ellenberg (EMBL) and Stefan Schönberg (EIBIR). The projected Euro-Biolmaging Preparatory Phase consortium comprises a set of 39 beneficiaries representing 15 ESFRI Member States. These partners represent leading scientists in the different imaging technologies and infrastructures as well as key political and funding bodies. In addition, Euro-Biolmaging has assembled a valuable set of more than 80 associated partners representing 23 ESFRI Member States and received 125 "letters of intent" from universities, research councils, ministries, funding organizations and industry.

Beneficiaries	Interest expressed by:	Associated partners
<ul style="list-style-type: none"> <li>- European Molecular Biology Laboratory, EU</li> <li>- EIBIR Gemeinnützige GmbH zur Förderung der Erforschung der Biomedizinischen Bildgebung, AT</li> <li>- Åbo Akademi, FI</li> <li>- Aarhus Universitetshospital, Skejby, DK</li> <li>- Fundacio Privada Clinic per a la Recerca Biomedica, ES</li> <li>- Fundacio Privada Centre de Regulacio Genomica, ES</li> <li>- Erasmus Universitair Medisch Centrum Rotterdam, NL</li> <li>- École Polytechnique Federale de Lausanne, CH</li> <li>- Helmholtz-Gemeinschaft Deutscher Forschungszentren e.V., DE</li> <li>- Istituto Europeo di Oncologia Srl, IT</li> <li>- Institute of Molecular Genetics – Academy of Sciences of the Czech Republic, CZ</li> <li>- Ludwig-Maximilians-Universität München, DE</li> <li>- Max Planck Gesellschaft zur Förderung Der Wissenschaften e.V., DE</li> <li>- Universitätsklinikum Freiburg, DE</li> <li>- Università degli Studi di Torino, IT</li> <li>- University of Dundee, UK</li> <li>- Universitat Pompeu Fabra, ES</li> <li>- Weizmann Institute of Science, IL</li> <li>- Westfälische Wilhelms-Universität Münster, DE</li> <li>- The Netherlands Organisation of Health Research and Development, NL</li> </ul>	<ul style="list-style-type: none"> <li>- Austrian Federal Ministry of Science and Research (AT)</li> <li>- Belgian Science Policy Office (BE)</li> <li>- Ministry of Education Youth and Sports (CZ)</li> <li>- German Federal Ministry of Education and Research (DE)</li> <li>- Bavarian State Ministry of Sciences, Research and the Arts (DE)</li> <li>- German Research Foundation (DE)</li> <li>- Danish Agency for Science, Technology and Innovation (DK)</li> <li>- Spanish Ministry of Science and Innovation (ES)</li> <li>- Generalitat de Catalunya (ES)</li> <li>- Finnish Ministry of Education (FI)</li> <li>- CEA, INSERM, CNRS, INRIA (FR)</li> <li>- National Office for Research and Technology (HU)</li> <li>- Israel Science Foundation (IL)</li> <li>- Ministero dell'Istruzione, Università e Ricerca (IT)</li> <li>- Regione Piemonte (IT)</li> <li>- National Research Council of Italy (IT)</li> <li>- Dutch Ministry of Education, Culture and Science (NL)</li> <li>- Research Council of Norway (NO)</li> </ul>	<p>82 organizations have expressed their interest to actively participate in the Euro-Biolmaging working groups as Associated Partners.</p> <p><b>Countries:</b>            Austria: 4            Belgium: 2            Switzerland: 1            Croatia: 1            Czech Republic: 6            Germany: 10            Denmark: 2            Estonia: 1            Spain: 3            Finland: 3            France: 7            Greece: 8            Hungary: 1            Ireland: 2            Italy: 7            Netherlands: 6            Norway: 1            Poland: 4            Portugal: 1            Sweden: 5            Slovenia: 1            United Kingdom: 7            Israel: 1</p>

<ul style="list-style-type: none"> <li>- Agencia D'avaluació de Tecnologia i Recerca Mèdiques, ES</li> <li>- Commissariat a l' Energie Atomique, FR</li> <li>- Deutsche Forschungsgemeinschaft, DE</li> <li>- Eidgenössische Technische Hochschule Zürich, CH</li> <li>- Imperial College of Science, Technology and Medicine, UK</li> <li>- Otto-Von-Guericke-Universitaet Magdeburg, DE</li> <li>- Universitair Medisch Centrum Utrecht, NL</li> <li>- Friedrich Miescher Institute for Biomedical Research, CH</li> <li>- European Organisation for Research and Treatment of Cancer, BE</li> <li>- Instytut Biologii Doswiadczalnej im. M. Nenckiego Polskiej Akademii Nauk, PL</li> <li>- Biotechnology and Biological Sciences Research Council, UK</li> <li>- Consiglio Nazionale delle Ricerche, IT</li> <li>- Fraunhofer-Gesellschaft zur Foerderung der Angewandten Forschung E.V, DE</li> <li>- Nederlandse Organisatie voor Wetenschappelijk Onderzoek, NL</li> <li>- Institut National de la Sante et de la Recherche Medicale, FR</li> <li>- Institut National de Recherche en Informatique et en Automatique, FR</li> <li>- Uppsala Universitet, SE</li> <li>- Centre National de la Recherche Scientifique, FR</li> <li>- Ruprecht Karls Universitaet, Heidelberg, DE</li> </ul>	<ul style="list-style-type: none"> <li>- Polish Ministry of Science and Higher Education (PL)</li> <li>- Ministerio da Ciencia, Tecnologia e Ensino Superio (PT)</li> <li>- Swedish Research Council (SE)</li> <li>- Medical Research Council (UK)</li> <li>- Wellcome Trust (UK)</li> <li>- Republic of Croatia - Ministry of Science, Education and Sports (HR)</li> <li>- Ministry of Education, Life Long Learning and Religious Affairs (GR)</li> </ul>	
<b>8. Costs for construction, operation and decommissioning, indications on project financing.</b>		
<p>One of the main goals of Euro-Biolmaging is to maintain and extend its competitiveness in imaging technologies. The required investment is high and should be in addition to funds allocated to basic research and not part of it. The use of such an investment through a coordinated plan well integrated into the current and future European research landscape will have significant advantages. First, the investment can be more targeted so that the cutting edge technology is not duplicated unnecessarily in each Member State. Second, the dissemination of know-how and technology to constantly update and improve the infrastructures will be more efficient. Third, it will facilitate the use of shared resources and standards (algorithms, data standards, compute processing power, databases).</p>		

**1. Preparatory Phase.** The objectives are

- to define the needs of the biomedical imaging user communities,
- to develop a plan for harmonised/standardised access to imaging technologies,
- to develop a plan for harmonised/standardised training curricula in imaging technologies,
- to develop a plan for image data management, storage and processing,
- to define the legal, governmental and financial framework for the construction and operation,
- to develop an overall business and construction plan based on the legal framework and finance plan

**2. Construction Phase.** Euro-Biolmaging infrastructure will be established and either newly constructed or set up through major upgrades of existing facilities.

**3. Operation.** Euro-Biolmaging will provide access and training to users. Technology will be kept state of the art through continuous technology evaluation and development and through continuous upgrades of instrumentation.

Total preparatory cost  
~ 7,9 Mio €

Total construction cost  
~ 600 Mio €  
  
to be further  
determined in the  
Preparatory Phase

Operation cost /year  
~ 250 Mio €  
  
to be further  
determined in the  
Preparatory Phase

Decommissioning  
cost  
  
Not applicable

**9. Timetable for construction, operation and decommissioning with duration and possible starting dates.**

Preparatory phase  
2010-2013

Construction phase  
2013-2017

Operation phase  
> 15 years


Decommissioning  
Not applicable

**10. Reference: Person who has submitted the proposal and will follow up in ESFRI.**

**Dr. Jan Ellenberg**  
European Molecular Biology Laboratory (EMBL)  
Meyerhofstr. 1  
D-69117 Heidelberg  
Germany  
T +49-6221-387-328  
F +49-6221-387-98328  
[jan.ellenberg@embl.de](mailto:jan.ellenberg@embl.de)

**Prof. Stefan Schönberg**  
European Institute for Biomedical  
Imaging Research (EIBIR)  
Neutorgasse 9  
A- 1010 Vienna  
Austria  
T +43 1 533 40 64-538  
F +43 1 535 70 41  
[stefan.schoenberg@medtech.uni-heidelberg.de](mailto:stefan.schoenberg@medtech.uni-heidelberg.de)

**Table 17: Links between Research Infrastructures – Euro-Biolmaging**

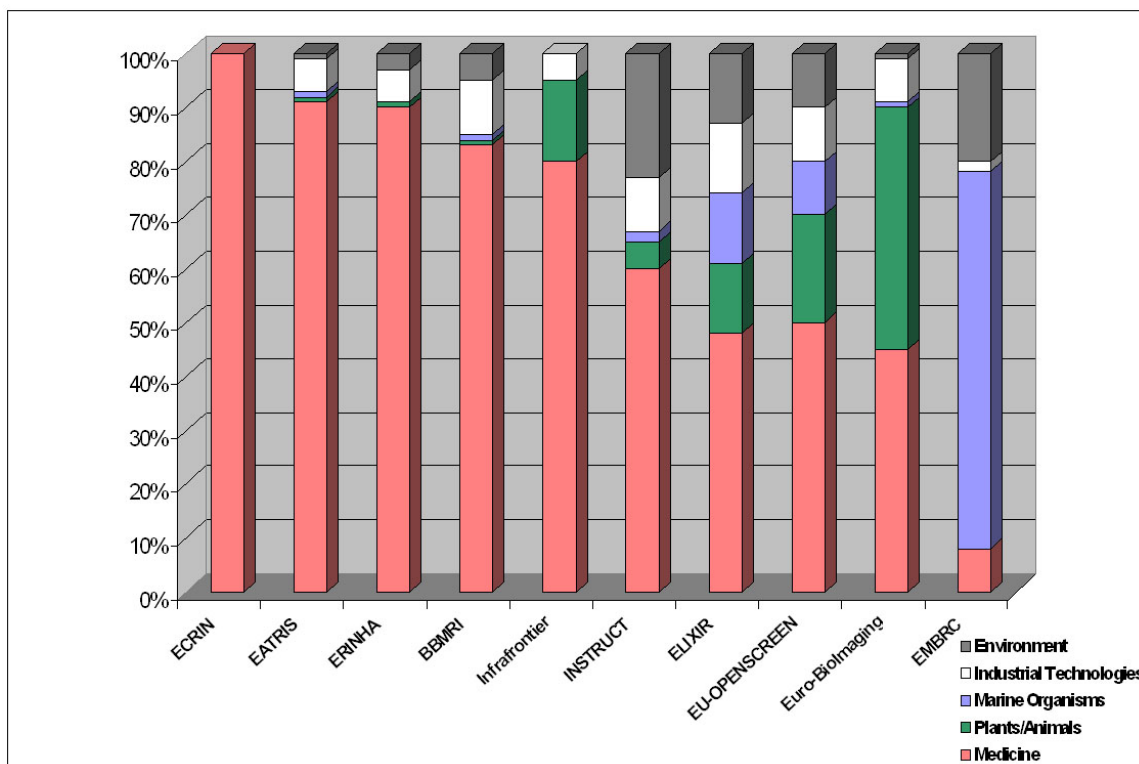
	Euro-Biolmaging	Further specification of the technological link	Further specification of the thematic link	Short statement for further specification (last update July 2010)
BBMRI		cooperative image - tissue data bases	correlation of new image markers with histopathological data	Euro-Biolmaging will provide innovative image analysis tools for the development of biomarkers and standards for image databases.
EATRIS		Technologies for image-based verification of disease mechanisms and therapeutic strategies, exchange on innovative imaging technologies, best practices and standardized protocols for biomedical imaging.	Access to state-of-the-art imaging analysis platforms for evaluation of preclinical data and monitoring of clinical studies.	Imaging in preclinical and clinical evaluation of new diagnostics and therapies, Euro-Biolmaging will provide access to imaging services and standards for methods, data, and user training to support the translational link between preclinical and clinical studies
ECRIN		development of surrogate image-based markers for earlier response assessment	clinical studies with standardized imaging for evidence-based diagnosis, assessment of therapeutic response and outcome	Euro-Biolmaging will work on the establishment of new quality standards for clinical trials with imaging technologies using established and new imaging biomarkers at the European level
ELIXIR		common standards for image data formats; technical links between public image and sequence data bases		A common node for image databases and public repositories could be set up within the ELIXIR RI to avoid duplicated efforts and profit from synergies
Infrafrontier		access to cutting-edge small animal imaging devices	imaging studies for diseases mechanisms and new therapeutic approaches in animals	Collaboration on imaging methods for mouse models, e.g. by establishing common imaging programs, common imaging technology development for small animals
INSTRUCT		correlative and structural imaging methods	Bridging resolution gaps of imaging methods. Identification of new imaging technologies to augment existing structure determination infrastructures.	Development of a common node for correlative light and electron microscopy
EMBRC		access to imaging technologies and devices for marine organisms	evaluation of marine organism models for imaging	Collaboration by offering services in imaging methods for marine organisms, e.g. by establishing common imaging programs
ERINHA		access to imaging technologies and devices for cells and pathogens	capacities development of cell and tissue imaging adapted to the needs of BSL4 laboratories	Euro-Biolmaging plans to evaluate deployment of an imaging infrastructure into high security laboratories in collaboration with ERINHA and a joint survey of pathogen and imaging communities will be conducted
EU-Openscreen		image capture and analysis of morphological or reporter signals in cell-based screening assays (high-content screening) is becoming an important alternative to single target in vitro screening assays	image-based high-content screening and drug profiling	Euro-Biolmaging plans a combined infrastructure for high throughput microscopy and chemical screening facility
e-IRG		explore remote image data storage and processing		Euro-Biolmaging and Infrafrontier plan together with EUDAT a pilot project to define requirements and explore solutions for an image warehouse that provides fast and distributed access and includes tools for navigation, visualisation, and annotation of image data.
SSH				
ESP				
ENV				
ENE				

#### 4.7 Contribution of RIs to different science fields

Although it is difficult to give a comprehensive diagrammatic presentation of the research activities of each BMS RI, the following diagrams broadly illustrate BMS RI participation across different

scientific fields and the contribution of each RI to research activities within the dominant field.

Figure 30 illustrates BMS RI activities in the research themes of environment, industrial technologies, marine organisms, plants/animals and medicine.



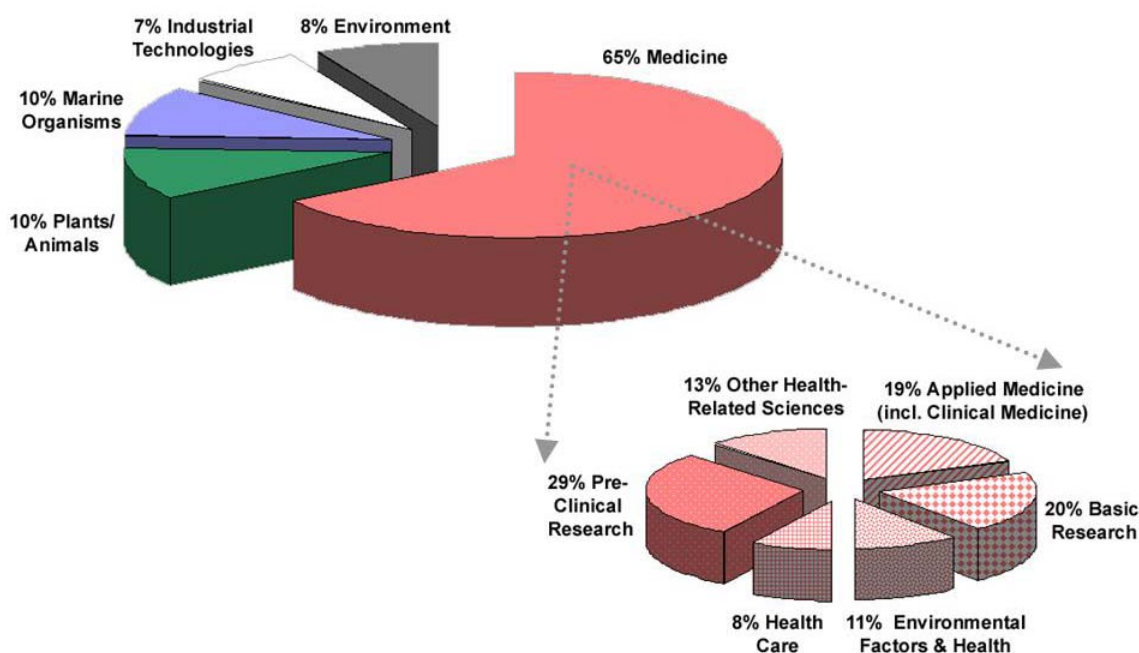
**Figure 30:** BMS RI activities in the research themes of environment, industrial technologies, marine organisms, plants/animals and medicine

The 6 first generation BMS RIs – ECRIN, EATRIS, BBMRI, INFRAFRONTIER, INSTRUCT, ELIXIR – are predominately active in the research area of medicine. With the exception of ELIXIR (45% participation) activities in medicine within each of the other 5 initiatives stands at over 50% of the total research activity of each RI.

The 4 second generation BMS RIs – ERINHA, EU-OPENSREEN, Euro-BioImaging, EMBRC – again show active participation in medicine; however EU-OPENSREEN, Euro-BioImaging and EMBRC also strongly contribute to the research themes of plants/animals and marine organisms (see Figure 30).

Overall, medicine is the dominant research activity for all 10 BMS RIs; they contribute a combined 65% of total research activity to this field. The combined activity for the 6 first generation BMS RIs in Medicine is 75%.

The research theme of medicine covers a broad spectrum of activities. Figure 31 illustrates an estimate of the contribution of each individual BMS RI to research activities across this spectrum, from basic medical/biological research and innovation activities to activities dedicated to health care. Not surprisingly the percentage of basic research is high, in accordance with the horizontal nature of several of the BMS RIs. The percentage of applied and translational activities is, however, increasing.



**Figure 31:** Estimate of each individual BMS RI to research activities across the medicine spectrum

#### 4.8 Common activities of BMS RIs

Some of the common activities of the 10 BMS RIs are already mentioned in Chapter 2: their networking with the BMS TWG as well as in Chapters 4.2 and 4.3: showing the thematic and technological links between the BMS RIs and other RIs of the Thematic Working Groups. As the BMS RIs show different interfaces between each other and with RIs of other TWGs, even overlaps, they are in a continuous dialogue.

A special meeting was organised with the e-Infrastructure Reflection Group, to discuss in depth the issues of data collection, storage, management and access. Strengthening of existing networks and the strategic planning of new cooperations was a most appreciated result of the meeting.

For embedding BMS RIs into the scientific landscape, the BMS RIs have created and submitted several joint proposals for transnational and EU funding.

Mutual relationships have as well been developed in the frame of the Preparatory Phases for RIs, financed by the European Union and are foreseen within other common measures of the Specific

Programme Capacities, esp. Integration Activities – see overview on the progress of the 10 BMS RIs.

As the 6 BMS RIs of the first generation cover a broad spectrum of competencies from molecules to humans, they took part in the first call for proposals of the Joint Undertaking Innovative Medicines Initiative. Together with the industrial project partners they succeeded and are establishing a pan-European platform for education and training comprising the whole lifecycle of medicines from basic research through clinical development to pharmaco-vigilance (EMTRAIN, European Medicines Research Training Network – [www.emtrain.eu](http://www.emtrain.eu)).

Another common activity of the BMS RIs is an application for the call INFRA-2011-2.3.2 “Implementation of common solutions for a cluster of ESFRI infrastructures in the field of Life Sciences” within the frame of the Specific Programme Capacities. The European Commission's main objective of this call is to support the common needs of projects in the same field. An EU financial support will be provided, through a targeted approach, to clusters of ESFRI infrastructures for their implementation phase. This support is aiming at



implementing common and efficient solutions on issues ranging from architecture of distributed infrastructures to distributed access management, from development of critical components to new/revised data acquisition, access and deposit policies.

In addition to the presentation of BMS RIs on the occasion of highly recognised scientific conferences or rather stakeholder oriented congresses and conventions (ECRI 2010) the BMS RIs contributed to and participated in several workshops and seminars.

Legal and financial issues were of utmost interest, as the implementation of the new legal instrument ERIC is progressing. Several meetings took place, where the conception of ERIC, its implementation structure and most recent developments were presented and intensely discussed.

The funding environment – be it for construction or operation – was the focus of a variety of events. Different schemes and models were discussed with relevant stakeholders and programme managers and/or owners.

The exchange of experiences gained during the ESFRI as well as national roadmap (update) processes and the Preparatory Phases for single RIs motivated the BMS RIs to jointly act with regard to future RI planning and decision making processes on a European level. Envisaging the future challenges Europe is facing the group of BMS RIs identified needs and requirements for RIs. BMS RIs jointly published a Strategy Paper. They detailed the benefit, contribution to and perspectives of BMS RIs within the European Research Area. In formulating a strategy addressing European decision makers, they are asking for i) strengthened capacities and fostered implementation of Research Infrastructures as a major pillar of the knowledge triangle –

science, training and innovation, ii) coherent and adequate funding strategies and instruments for integrating RIs sustainable into the research and innovation scenery. BMS RIs presented their Strategy Paper in Brussels on the 25<sup>th</sup> October, 2010 to Members of the European Parliament, to key decision makers within the European Commission and to the members of the Research Council Working Group.

#### 4.9 Conclusions

One of the main objectives of the BMS TWG is to support ESFRI in performing its incubator role for the RIs on the Roadmap. The whole ESFRI process will only be successful if the RIs on the Roadmap see the light of day. Therefore the BMS TWG concentrated very much on implementation and the bottlenecks which the RIs have to overcome on their way to reality. All BMS RIs are progressing excellent and evolving satisfactorily.

An important part of this development was an intense exchange of best practise between the 6 first generation RIs (BBMRI, EATRIS, ECRIN, ELIXIR, INFRAFRONTIER, INSTRUCT) of the 2006 ed. of the ESFRI Roadmap and the 4 second generation RIs (EMBRC, Euro-Biolmaging, ERINHA, EU-OPENSREEN) of the 2008 ESFRI Roadmap. The scientific coordinators of the 10 RIs not only met upon invitation of the BMS TWG in special meetings together with the BMS TWG members, but also at workshops to exchange their experiences with PPs. Within this frame the BMS RIs jointly developed strategies to intensify their mutual collaboration and cooperation activities. Table 18 gives a compiled overview of the networking between the BMS RIs, differentiated in technological and thematic links that are further specified in the presentation of each BMS RI.

**Table 18:** Links between the Research Infrastructures

	BBMRI	EATRIS	ECRIN	ELIXIR	Infrafrontier	INSTRUCT	EMBRC	ERINHA	Euro-Biolmaging	EU-Openscreen
BBMRI										
EATRIS										
ECRIN										
ELIXIR										
Infrafrontier										
INSTRUCT										
EMBRC										
ERINHA										
Euro-Biolmaging										
EU-Openscreen										
e-IRG										
SSH										
ESP										
ENV										
ENE										

Thematic link (with further specification)
Technological link (with further specification)
1 <sup>st</sup> generation RI
2 <sup>nd</sup> generation RI
Other ESFRI Groups
Direction of link: (uni-/bidirectional)

## 5 EVALUATION OF NEW PROPOSALS

### 5.1 Evaluation Procedure

ESFRI designed a stage-gate process to ensure that all initiatives to be reviewed by the respective Thematic Working Group for the update of the ESFRI Roadmap are assessed using the same transparent and fair procedure. The approach of this process is to review the Research Infrastructure concept and to judge the maturity of proposals (see Figure 32 for detailed information about the particular steps of the ESFRI stage-gate process).

For the 3<sup>rd</sup> time in series ESFRI launched a call for new initiatives to be considered for an update of the ESFRI Roadmap. The call in September 2009 invited proposals for new (or major upgrades of) RI initiatives of pan-European relevance in the specific fields of food, agriculture and fisheries, biotechnology (including systems biology) to be evaluated by the BMS TWG. The deadline for sub-mission was 31<sup>st</sup> December, 2009 (see Figure 32 “ESFRI stage-gate process - step 1”).

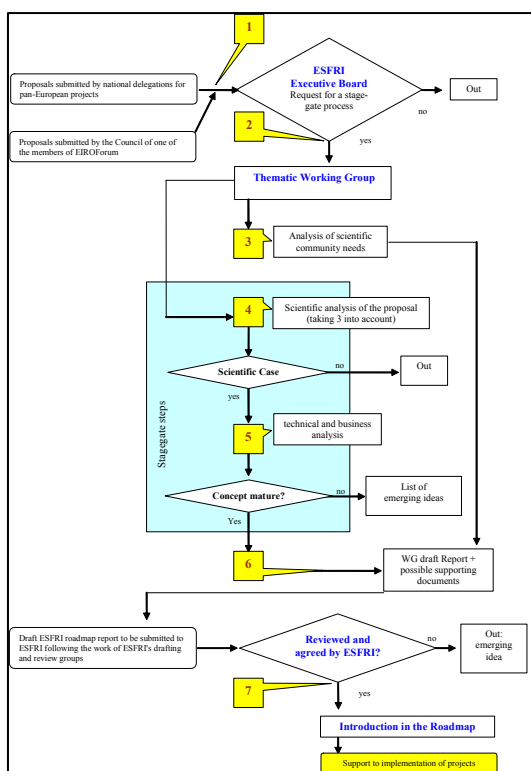
The ESFRI Executive Board (EB) forwarded 9 proposals to the BMS TWG (RU09\_01, \_09, \_10, \_17, \_18, \_19, \_20, \_21, and \_22; see detailed information in Appendix E “List of proposals received and assessed”). After a first screen and discussion between the EB and the BMS TWG Chair in January 2010, the proposals RU09\_18 (Euro-QUAM) and RU09\_19 (BIO3MASS) were considered to be out of the scope of the BMS Group. The proposal RU09\_21 (BRIDGE) was evaluated by the BMS TWG notwithstanding the fact that there were serious doubts whether this proposal was still within the scope of the BMS Group. The Danish ESFRI Delegation had submitted proposal RU09\_05 (BIOPRO), but withdrew it before the EB forwarded the proposal to the BMS TWG for evaluation (see Figure 32 “ESFRI stage-gate process - step 2”).

After a call for (re-)nominations of members of all TWGs ESFRI Forum decided about the composition of the BMS TWG. The members of the BMS Group are both science policy makers and scientific experts (Appendix A). Any potential conflicts of interest were dealt with according to the ToR of Thematic Working Groups, last updated on 12<sup>th</sup> June, 2009.

Since November 2007 a password protected working platform (created by the BMS TWG secretariat) is provided to all BMS TWG members. This platform contains all documents that are generated by the BMS Group (e.g. agendas and minutes of the meetings, proposals to be evaluated, assessment forms and guidelines, etc.) and is continuously updated by the BMS TWG secretariat. In order to ensure clarity and transparency of the procedure, all BMS TWG members have restricted access to the working platform

Three independent Expert Groups (EGs) covering the respective scientific areas of the proposals were established by the BMS TWG to ensure and maintain the high quality standard of the evaluation process in ESFRI.

All Expert Groups were chaired by a BMS TWG member, who reported directly to the BMS Chair and the BMS Group. Each



**Figure 32:** Overview about the ESFRI stage-gate process for the update of the ESFRI Roadmap 2010

Expert Group consisted of up to six members (including the Expert Group Chair).

The Expert Group “Systems Biology” was only composed of internal experts (from BMS TWG) whereas the Expert Groups “Biorepositories – Microorganisms” and “Green Biotechnology & Biological Sciences” consisted of external experts in addition to the respective Chair. A representative of the ENV TWG was included in the latter EG. In addition to the membership of a representative of ENV TWG the Chair of ENV TWG also sent comments in writing.

The external members of each Expert Group were nominated by the BMS TWG following recommendations of acknowledged professionals in the specific areas of science against the background of their reputation and expertise. Moreover, the balance of countries and gender was taken into account and any possible conflict of interest was excluded. The membership in the Expert Groups embraced some of Europe’s and the world’s leading biologists and medical scientists.

The following three Expert Groups were set up:

Expert Group 1: “Systems Biology” (chaired by Professor Stig Omholt, NO)

Expert Group 2: “Biorepositories – Microorganisms” (chaired by Professor Andres Metspalu, EE)

Expert Group 3: “Green Biotechnology & Biological Sciences” (chaired by Dr. Ester Serrão, PT)

The Expert Groups worked from January 2010 to May 2010. On 8<sup>th</sup> April, 2010 there was a one-day Consensus Meeting in Bonn, where all three different Expert Groups came together to discuss their results and prepared final recommendations to the BMS TWG. In its work, the Expert Groups followed the set “Procedural Guidelines for BMS Expert Groups”.<sup>12</sup>

The EGs have reviewed the needs of the biological and medical scientific communities for pan-European infrastructures and analysed the specific proposals received through ESFRI. The EGs reviewed the proposals for new Research Infrastructures or major upgrades of pre-existing Research Infrastructures and prepared recommendations for the BMS TWG.

### 5.1.1 Procedural guidelines for BMS Expert Groups

#### Chair of an Expert Group:

The Expert Groups were chaired by members of the TWG. The Chair of an Expert Group should not be involved in a specific Research Infrastructure to be evaluated by this Expert Group.

He/she was responsible for the timetable and good organisation of the evaluation process.

The BMS secretariat supported the Chairs if required.

#### Membership:

The members of the Expert Groups should not be involved in a specific RI proposal neither as coordinator nor as possible partner. Any conflict of interest shall be reported right at the beginning of the evaluation procedure to the Chair of the Expert Group.

Members of the Expert Groups were selected on the basis of their expertise, including science policy development, and of their international reputation.

An Expert Group consisted of no more members than it was necessary to provide an overview of the area under consideration; Expert Groups ideally had up to six members.

The BMS TWG Chair could announce another expert in case one of the approved experts was not available, following a consultation with the Chair of the respective Expert Group.

<sup>12</sup> Remote Evaluation Process; Update of the Roadmap Research Infrastructures Thematical Working Group Biological and Medical Sciences; Procedural Guidelines for BMS Expert Groups

#### Method of working:

Members of the Expert Groups performed evaluations on a personal basis and did not represent their national or private interests. They were expected to be independent, impartial and objective, and to behave throughout in a professional manner.

A meeting of the Expert Groups to discuss their findings was held in a closed-session; all information exchanged within and prepared by the Expert Group was meant for internal use only, unless explicitly stated.

#### Basic requirements for consideration:

Under supervision of the BMS TWG, the Expert Groups assessed if a potential (major upgrade/new) pan-European Research Infrastructure should be included in the Roadmap or not.

To fulfil their tasks, and before analysing specific initiatives (which should have received the previous support of an ESFRI member), the Expert Groups reviewed, on the basis of existing information, the needs of the potential user scientific community(ies) within the next 10 to 20 years (see Figure 32 "ESFRI stage-gate process - step 3").

Each identified Research Infrastructure was reviewed according to two main criteria of the stage-gate process for evaluation of new proposals laid down by the ESFRI Forum:

### **The Scientific and the Concept Case**

1. The **Scientific Case** (see Figure 32 "ESFRI stage-gate process - step 4"): The proposed new RI should correspond to future needs of the scientific communities in Europe, demonstrate impacts on scientific developments, support new ways of doing science in Europe and participate to the enhancement of the European Research Area.

Additional information, supported by the appropriate scientific community at European level, should demonstrate its pan-European value, setting the scene for the infrastructure in a European and an international context, as well as its relevance and quality.

2. The **Concept Case** (see Figure 32 "ESFRI stage-gate process - step 5"): The proposed new RI should be technologically and financially feasible and meet the necessary degree of maturity which is defined as (a) the existence of a technical concept for the realisation of the RI and of feasibility studies, including identification of technical challenges and risks, (b) the existence of a projection about construction, operating and decommissioning costs, including a clear timetable. In addition, ESFRI analysis requires relevant information on (c) the recent or near future peer review of the RI, and by which panel; (d) the potential for risks- and costs-sharing and for developing effective joint actions in Europe; (e) the mechanisms for other partners to join later on and (f) the mechanisms to ensure the human resources and the capability to use the RI in the most open and effective way.

#### **5.1.2 Modus operandi**

The Chair of the BMS TWG provided information covering the evaluation procedure, the experts' responsibilities, the issues involved in the particular area/objective, and assessment forms.

The first part of the evaluation (until 15<sup>th</sup> March, 2010) was carried out on the premises of the experts concerned ("remotely").

In this first step the experts were acting individually. The experts recorded their individual opinions in an Individual Assessment Report (IAR); concise but explicit justifications were given for each score and also comments against the evaluation criteria.

The experts further collected questions they identified as not sufficiently described in the proposal template as well as recommendations for improvements if useful and sent it to the Chair of the Expert Group, who then clarified these issues with the coordinator of the proposal and provided a suitable feedback to the members of the Expert Group.

Based on this feedback information the experts provided suitable comments to be discussed at the Expert Group meeting (see

below). All experts completed their IAR and sent it to the respective Chair of the Expert Group.

The second step included a Consensus Meeting in Bonn (8<sup>th</sup> April, 2010), at which the experts presented their views, discussed and prepared comments for the particular RIs relating to the scientific landscape. Finally they produced one final common assessment form for each proposal.

The discussion was moderated by the Chair of each Expert Group. He/she sought to arrive at a consensus between the individual views of experts without any prejudice for or against particular proposals or the organisations involved.

The Chair was responsible for drafting the final evaluation report, which also contained scores and comments from the final assessment form. The Expert Groups also came to a common view with respect to the scientific landscape.

The final evaluation report was provided to the BMS TWG Chair for discussion in the BMS TWG meeting in June, 2010.

### 5.1.3 Evaluation Criteria

The proposals were evaluated against pre-determined evaluation criteria.

Each criterion was scored out of 5. Half marks could be given. No weightings were applied. The scores indicated the following with respect to the criterion under examination:

0 - Insufficient: The proposal fails to address the criterion under examination or cannot be judged due to missing or incomplete information.

1 - Poor: The criterion is addressed in a cursory and unsatisfactory manner.

2 - Fair: There are serious inherent weaknesses in relation to the criterion in question.

3 - Good: While the proposal broadly addresses the criterion, there are significant weaknesses that would need correcting.

4 - Very good: The proposal addresses the criterion well, although certain improvements are possible.

5 - Excellent: The proposal successfully addresses all relevant aspects of the criterion in question. Any shortcomings are minor.

The following criteria were checked to assess the maturity of the 7 proposals to be evaluated:

#### Scientific Case:

- Does the proposed RI offer an important service responding to the future needs of users?
- In how far does the proposed RI address the needs of European/global users within the given field?
- Is/are the target group(s) of users identified?
- Will the proposed RI contribute to the excellence and coordination of high-quality work in Europe?
- Is the pan-European/global value clearly demonstrated?
- Please clarify how the new RI will fit into the existing and future landscape of research and of existing RIs.
- Does the proposed RI offer an improvement beyond the state of the art?
- In how far does the proposed RI contribute to the problems to be solved?
- In how far does it contribute to harmonisation and standardisation within Europe?

#### Concept Case:

- Is the necessary scientific and technological expertise identified?
- Is the concept technologically feasible?
- Is the requirement for e-infrastructure sufficiently described?

- Can it be integrated with the existing EU e-infrastructure?
- Are the important key players identified and integrated in the proposed RI?
- Are costs estimates feasible?

#### Additional questions:

- In how far does the proposed RI contribute to innovative research/innovation/demonstration, training and other relevant activities?
- Has the proposed service and/or access for users to the RI been made clear?
- Would you have recommendations for the proposed RI?

## 5.2 Evaluation Results

All 7 proposals were available for the BMS TWG members from the password-protected BMS working platform during the process of evaluation. The recommendations prepared by the Expert Groups were taken into account during the 5<sup>th</sup> BMS TWG meeting in Paris on 16<sup>th</sup>/17<sup>th</sup> June, 2010, where all proposals were discussed and assessed.

The common final evaluation result of the Expert Groups was to recommend 3 of the applications as mature proposals: **ISBE** (Infrastructure for Systems Biology-Europe), **ANAEE** (Infrastructure for Analysis and Experimentation on Ecosystems) and **MIRRI** (Microbial Resource Research Infrastructure).

The BMS TWG unanimously agreed to the vote of the Expert Groups and identified 3 proposals as promising Research Infrastructure initiatives, which passed step 6 of the stage-gate process. BMS TWG is of the opinion that the 3 above mentioned proposals meet the ESFRI criteria for inclusion in the update of the ESFRI RM 2010 (see Figure 32 “ESFRI stage-gate process - step 6”). In the case of ANAEE BMS TWG welcomed a written understanding that the RI while progressing towards the Preparatory Phase would

enlarge its scientific community to strengthen the structuring effect.

Furthermore, the BMS TWG decided that 4 proposals did not pass step 5 of the stage-gate process and shall not be considered for the inclusion in the ESFRI RM 2010.

### 5.2.1 Mature Proposals

The proposals identified as being mature fully met the demands of major pan-European Research Infrastructures. They were well characterised by contributions to the excellence and coordination of high-quality work and innovative research in Europe when offering important services with regard to the future needs of European or global users. Furthermore, these initiatives clearly demonstrated an improvement in their respective scientific area beyond the state of the art in view of a pan-European/global value. An outstanding attribute of these future RIs was their notable contribution to harmonisation and standardisation within Europe not least as a result of their technologically feasible concept as well as the identification and integration of important target groups and players.

#### **RU09\_01 ISBE – Infrastructure for Systems Biology-Europe**

Submitted by the ESFRI delegation of the United Kingdom

##### Short description

Systems biology is a research methodology at the current frontier of the Life Sciences (basic and applied) - being used in fundamental biology, medicine and biological engineering. It represents a highly interdisciplinary approach to the understanding and harnessing of biological complexity. It builds upon the great advances triggered by the “-omics” revolution and it goes beyond them by combining high-throughput experimental approaches in molecular biology, biochemistry and chemistry with bioinformatics, novel physics and engineering technologies, together with sophisticated mathematical approaches with particular emphasis on modelling and simulation. Consequently, systems biology does not sit comfortably in any single

department or even a classical university faculty. It demands new intellectual and organisational structures to deliver its full potential. The proposal suggests the establishment of a concerted European systems biology infrastructure providing broad access to instrumentation, competence, computing facilities and repositories for enhancing the breadth and quality of systems biology research in Europe. Furthermore, this Research Infrastructure initiative provides a special feature in the European Research Area for the interconnection with other Research Infrastructures in the field of Life Sciences, e.g. ELIXIR.

#### Synthesis opinion

There is an unquestionable need for building a service infrastructure for systems biology research in Europe that can provide a broad spectrum of services enabling European researchers to better exploit the possibility window that has been opened by the combination of theoretical disciplines with dramatic improvements in sequencing and phenotyping technologies. The proposal has the potential to develop into a very strong, organisationally as well as thematically, concerted pan-European service infrastructure that will be enthusiastically supported by several Member States. Such a Research Infrastructure has to have a decentralised structure, and compared to the setup of a single service facility, this poses a series of additional challenges concerning sharing of responsibilities among service nodes, proper addressing of well documented needs, and proper integration of stakeholders that already have shown long-term commitments to building up relevant infrastructure for systems biology research as well as providing high-quality work within the field based on European funding. The current proposal represents a good point of departure for a successful handling of these challenges.

#### Justification in detail

A systems biological approach offers a wealth of opportunities to understand and utilise biological complexity rather than deconstruct it in a reductionistic mode. Along with its intellectual cousin synthetic biology, it is very important to the future of the European economy, e.g. in the pharmaceutical and biotechnology

industries. Currently, the US leads the world in many aspects of systems biology. For this reason there is an urgent need in Europe to establish new organisational structures that facilitate the sharing of knowledge and expertise, seamless exchange of data and models, and the creation of new targeted educational programmes. This is the proposed role of ISBE, a distributed infrastructure aimed at providing coherence, critical mass and focus within Europe, to promote best practice, standardisation and joint working - maximise return on investment and enable the realisation of large-scale integrated research programmes.

#### **RU09\_09 ANAEE – Infrastructure for Analysis and Experimentation on Ecosystems**

Submitted by the ESFRI delegation of France

#### Short description

ANAEE aims at developing a coordinated set of state of the art experimental platforms to analyse and predict the responses of ecosystems to environmental changes and to engineer management techniques to deal with these changes. This will be achieved by setting-up a distributed and coordinated network of well equipped state of the art *in situ* and *in vitro* experimental platforms associated with analytical and modelling platforms and linked to networks of instrumented observation sites.

*In situ* long-term experimental platforms will be distributed across the main types of climate and land use. Experimental approaches will assess effects of land management, climate and biodiversity. Long-term continuous measurements will be recorded for state variables of the system in conjunction with the biogeochemical cycles, fluxes to hydrosphere and atmosphere and the dynamics of biodiversity. A few Ecotrons, highly instrumented, will allow deepening our understanding of processes and testing specific combinations of forcing variables. Analytical platforms at the cutting edge of technological development will quantify the complex interactions between the different matter cycles, ecological states and compartments, complemented with data base and modelling platforms.



### Synthesis opinion

ANAE will provide services that are strongly needed for excellent research on food and animal production ecosystems but it is additionally also very useful to address ecological, environmental, biodiversity and human health questions. This is considered a logical and very positive aspect, because the issues of food and animal production cannot be addressed separately from these, but rather in a complementary and coordinated manner as can be achieved in this infrastructure. In this way, such an infrastructure will also offer a bridge between biological and environmental scientific communities. A major need in agricultural research is to integrate experimentation with large temporal and spatial scales relevant to the most pressing future drivers to achieve a better and more holistic understanding of the underlying processes. The availability of experimental facilities, very large data sets and the multi-functional measurements and observations of complementary platforms will allow a novel understanding of the dynamics of the state and fluxes within and between the most relevant compartments across a hierarchy of spatial and temporal scales. It will therefore contribute to the pan-European integration of sciences and will bridge the existing research gap between monitoring and observational and functional experimental approaches, fully integrated towards modelling and prediction.

### Justification in detail

ANAE targets the need for long-term Research Infrastructure to address important European and global future scientific needs, namely the biological and ecological understanding of processes related to biomass production, including food, fibre and fuel - agriculture, food security and climate change.

This proposal's strength is the very good integration at all levels. The holistic approach of ANAE clearly offers an important improvement beyond the state of the art. Integration of different scientific fields, approaches and methodologies, actors and users, as well as with other infrastructures and with closely related networks will result in a much greater integrated potential than the sum of its individual parts. It also has clear pan-

European value, providing a significant enhancement of Europe's capacity. The envisaged collaboration with other infrastructures and networks will have an outreach function for the science fields concerned well beyond the European borders. The *in situ* long-term experimental platforms when integrated, will provide a novel understanding of the complex interactions between the different cycles, ecological states and compartments, allowing to evaluate, predict and assess the effects of climate change and land use on ecosystem processes.

Major actors and users as well as the respective target groups are identified within the different scientific areas, resulting in sound potential for future use and development. It is recommended that the partnership should be open to provide a stronger European balance regarding the expertise, climate zones, soil types, and in the final organisational and management structure due consideration should be given to access policies and dissemination activities for an effective and efficient scientific use of this infrastructure.

ANAE requires a long-term scientific commitment which will require a long-term financial commitment for the running costs, and efforts to develop a business-model are required.

### **RU09\_10 MIRRI – Microbial Resource Research Infrastructure**

Submitted by the ESFRI delegation of France

### Short description

MIRRI brings together European microbial resource collections with stakeholders aiming at improving access to enhanced quality microbial resources in an appropriate legal framework. It will build the European platform within the future Global Biological Resource Centre Network (GBRCN) for microorganisms. Microorganisms and their derivatives are the essential raw material for the advancement of biotechnology, human health as well as research and development in the Life Sciences. Products derived from microorganisms include drugs, antimicrobials, biopesticides and industrial enzymes. Uses include biocontrol, biofuel

production and direct use as food. Better-managed resources will lead to further discovery in all areas of the Life Sciences including healthcare.

MIRRI builds on several initiatives and activities respectively in this area: the Organisation for Economic Co-Operation and Development Biological Resource Centre (OECD BRC) Task Force providing best practice, the GBRNC demonstration and the European Consortium of Microbial Resources Centres (EMbaRC) projects, voluntary scientifically based collection network activities, such as World Federation for Culture Collections (WFCC) and European Culture Collection Organisation (ECCO). MIRRI enhances existing European microbial resource collections by linking them to third country partners extending globally.

MIRRI will improve quality and add value to the biological materials available for research, providing a comprehensive coverage of organisms and associated data. It will provide improved services to identify and characterise newly discovered strains that will help drive biotechnological research and place Europe at the head of microbial based innovation and bioeconomy development. MIRRI will complement ESFRI initiatives such as EMBRC (focussing on marine biodiversity, "blue" biotechnology), BBMRI (focussing on primary material of human origin, "red" biotechnology) and ERINHA (focussing on high pathogenic organisms) by concentrating on green and white/grey biotechnology sectors.

#### Synthesis opinion

This proposed RI is an excellent and mature proposal. National structures from all over the Europe are already established, scientific and technological expertise centres identified. MIRRI will offer services to different sectors like agriculture, biotechnology, food production, drug development, energy and healthcare. The proposed RI will contribute to excellence of research (coverage/best practice/global access plus standardisation of the resources) and human resource development incl. taxonomic expertise.

It is complementing the existing RIs (BBMRI, EATRIS, EMBRC) and requires

input/help from ERINHA and ELIXIR. It is really large, covering the whole Europe and well integrating into the EU e-infrastructure.

#### Justification in detail

The proposed RI will build on existing national RIs and international networks in order to build up a pan-European virtual RI. It demonstrates an extensive collaboration network. This RI is the correct infrastructure for developing the area of chemical biology: microbial metabolomics, metabolite profiling, detection and quantification of microbial toxins. Especially the toxins area is not covered by any of the present national culture collections, and yet this area has large potential as resource for therapeutics and drugs, which produces an interlinkage to the BMS RI EU-OPENSOURCE. There is a plan to develop future new technologies to exploit the European microbial resources and feed the innovation of bioactive molecule research and application. This RI will make microbial resources and materials available for the industry and supports the high quality research, training and education in Europe.

#### **5.2.2 Immature Proposals**

The proposals identified as being immature did not meet the criteria of major pan-European research. Some of the reasons to reject the proposals were in common to all proposals and others were very specific. In general they had a too narrow scope and were not as pan-European orientated as requested. In most of the cases a coherent management structure was missing. Furthermore, potential partners and key players were not sufficiently identified and the objectives were not well developed.

#### **RU09\_17 EABB – European Animal BioBanking Infrastructure**

Submitted by the ESFRI delegation of Italy

The rationale of this proposal is to construct the animal biobanks with a collection of biological samples, such as blood, tissues or DNA, plus associated epidemiological, clinical and research data. As such this would form an important objective.

The organisation behind this proposal "Istituto Zooprofilattico Sperimentale della

Lombardia e dell'Emilia Romagna" (IZSLER) is involved in highly specialised activities in the field of animal health, food and zootechnic hygiene. Experts are worried that the whole plan is presented from the viewpoint of IZSLER and Italy. It is lacking the true European dimension, which is a serious sign of pre-maturity of the proposal. Moreover, little information is given how this RI proposal will advance the European RIs beyond the state of art. The element of excellence is largely lacking and the target groups are not clearly identified. How this RI will fit into existing and future landscape of European RIs is not given. Experts are regarding this RI as a vision and not a mature RI proposal. This RI does not meet the standards necessary for inclusion in the update of the ESFRI RM 2010.

#### **RU09\_20 EMCSBI – European Mediterranean Crop Systems Biology Institute**

Submitted by the ESFRI delegation of Italy

The essence of this proposal is to set up a genomics research network focused on Mediterranean crops. The proposed institute appears to consist of groups currently participating in plant genomic projects involved in high-throughput sequencing. The proposal has a flavour of being a project rather than a RI. The proposal frames important research topics, though. But the suggested approaches are better characterised as belonging to standard functional genomics research than systems biology. Funding of such research is obtainable from several sources. The service element, the user profile and the pan-European element characterising a mature RI proposal are almost completely lacking.

However, the BMS TWG recommended the scientific coordinator of this proposal applying for appropriate calls within FP 7 to get support to promote the research programme suggested.

#### **RU09\_21 BRIDGE – Bioscience center for bridging laboratory with agro-ecosystem analysis for climate change adaptation research**

Submitted by the ESFRI delegation of Italy

The proposal BRIDGE aims to create an infrastructure to be used as a prototype and demonstrator for approaches to address climate change in agriculture.

The proposal is regarded as immature because it lacks sufficient focus and novelty to strongly improve European science. Although the biological questions are defined as important research topics, the proposal is not clear enough about what it is aiming for in terms of the needs of the future when addressing those questions. There is neither sufficient specification of the key scientific areas nor the key problems to be tackled. A major weakness of the proposal is the involvement of potential partners or key players – this is not sufficiently detailed. As the aims and objectives are not well developed there is insufficient information on the specific groups which should be involved; the required expertise is not identified. The different hubs are not specified clearly enough to show which kind of existing RIs they are intending to combine with and integrate. The basis for estimating the financing is not properly developed.

Nevertheless, the Expert Group recommended that the scientific coordinator of this proposal could attempt to integrate within ANAEE components of the research programme suggested. This would also help to create links to other European regions, overcoming the problem of having one single region where experimentation could be conducted.

#### **RU09\_22 MED.BANK – Mediterranean Biological Resources Center**

Submitted by the ESFRI delegation of Italy

This proposal aims to create a biological resource bank for the agricultural, food and energy sector with relevance for the problems of desertification in Mediterranean area. This is an important goal given future climate change predictions for Europe and the potential solutions to future warming and

drought-related problems that may be found in current Mediterranean biological resources.

Therefore this proposal addresses services and research topics that have the potential to be important on European level.

However, the proposal is immature with very significant limitations, because it does not provide enough information about the

scientific concepts, the methodologies and archiving technologies that will be applied, nor the integration of users and the research services that will be provided.

The EG requested additional information on these issues but obtained no answer from the proposal. A careful development of the scientific, technological and coordination plans and their contribution to excellence of work in Europe is needed in this proposal.

### 5.3 Mature Proposal Templates

**1. Descriptive title and information on the ESFRI delegation submitting the proposal (or one of the members of EIROForum).**

**ISBE**  
**Infrastructure for Systems Biology - Europe**  
 Submitted by the United Kingdom ESFRI Delegation

**2. Synthesis description of the new RI (or major upgrade) and S&T fields involved at pan-EU level in its use. Add links to relevant data/web pages.**

**Aim:** To integrate resources and expertise in systems biology across Europe, synergising effort and providing economies of scale, readily accessible by the European research community.

**Focus:** Detailed information on components of living systems continues to increase, but our ability to understand the dynamic interactions within systems remains a challenge. Hitherto it has not been possible to tackle this challenge effectively because of technical limitations and limited accessibility to a small number of specialised groups. This situation is rapidly changing and this is a timely opportunity to coordinate the distributed European research effort in systems biology within an infrastructure, the focus of which will be to enable researchers to (i) address how the interaction of biological components leads to the functioning of living organisms in a constantly changing environment, (ii) create models of living organisms at various scales representing these interactions, (iii) exploit this information to generate major socio-economic benefits in areas including healthcare, agricultural science and the environment.

**Structure:** ISBE will (i) interconnect hubs of technological excellence in systems biology, offering the best European research expertise, and experimental and modelling facilities, necessary for systems biology, (ii) establish and make available repositories of data and models, and (iii) enable real-time connections within and between components of (i) and (ii) and with external "user" laboratories, through the provision of high performance connections to existing high capacity electronic network infrastructures. Hubs will contribute specific skills and expertise to functional clusters focused on a variety of topics in an operational matrix, and some hubs may have groups that participate in different and/or multiple clusters. This structure will also facilitate efficient interaction with the substantial technology development efforts relevant to systems biology already funded by national programmes (e.g. BBSRC, BMBF, SystemsX.ch, EU, ERC), to enable the wider testing, validation and implementation of those emerging technologies, whilst simultaneously creating a demand for further critical technology development. ISBE will enable all European laboratories to model, conduct experiments and undertake other activities remotely, where they cannot be done locally, but which are required for their systems biology research programmes. This is an essential point because systems biology requires significantly more multidisciplinary facilities than are typically present in any single institute, industrial enterprise or even some Member States.

**Impact:** ISBE will enable broad and focused European research participation, tackling the grand challenge of developing a systematic understanding of complex biological processes in living organisms - including the human, and to develop and implement the necessary enabling technologies. The use of computer models and systems analysis will transform our current basic, fragmented knowledge of complex molecular systems into an integrated dynamic approach that can be applied across a variety of biological and biotechnological fields. These are as diverse as the evolving area of predictive, preventive and personalised medicine, biofuels and ecology. Further, efficient and real-time access to the best expertise and facilities across Europe will have a socio-economic impact on the less well-developed partner states

that have an interest in these areas, but which lack the necessary facilities to compete effectively in the field. The connections within ISBE will also create the opportunity for enhanced training and development of the necessary multidisciplinary skills at the postgraduate and post-doctoral level across all Member States. This will enable a more effective utilisation of human resources and human diversity across Europe and facilitate the involvement of new countries in the development and exploitation of this new discipline in science and technology. Wider dissemination of data, results and developments, to both the scientific and lay communities, will be undertaken using a variety of communication tools, beginning with the establishment of the ISBE website ([www.ISBEnet.eu](http://www.ISBEnet.eu)).

**3. Scientific Case: Scientific area(s) and potential and/or explicit users, how the new RI will fit into the existing and future landscape of research and of existing RIs, at EU and world level.**

Most biological processes involve network interactions between multiple genes, proteins and environmental variables. The complexity of these interactions in time and space is enormous, creating highly individual and variable responses. Attempting to unravel and understand the dynamics of these processes requires the collection and integration of experimentally-derived, quantitative, systems-wide data on the state, dynamics and variability of living cells, organs, organisms and populations. Handling and interpreting these diverse data sets demands the use of a variety of computational, mathematical and statistical modelling techniques and can only be achieved with a critical mass in both the experimental and quantitative sciences. Achieving this effectively to deliver the ultimate goal of understanding how biological function emerges from interacting biological components is the major challenge for modern biology and lies at the core of evolving systems approaches.

Biological research projects are no longer confined to single institutions covering all components of the project. Increasingly this involves collaborations between groups in various institutions, each with specific expertise and/or facilities working synergistically. Building on such experiences gained by European research consortia in systems biology, this integrated European infrastructure will exploit existing synergies and will create new opportunities for efficient research coordination and collaboration. ISBE will also make available cutting-edge technology in experimental and computational systems analysis to the wider community of European life scientists. Approximately 50 centres specialising in particular experimental and/or computational technologies will combine in a variety of operational clusters to create the backbone of the infrastructure. These centres will contribute to ISBE not just through cluster specific projects, but also through the training of researchers - and by acting as hubs for stimulating further technology development. Additionally, the ISBE centres will catalyse the broader integration of the quantitative sciences of physics, mathematics and engineering with biology by providing a unique environment where scientists from all these disciplines meet, work together and educate each other.

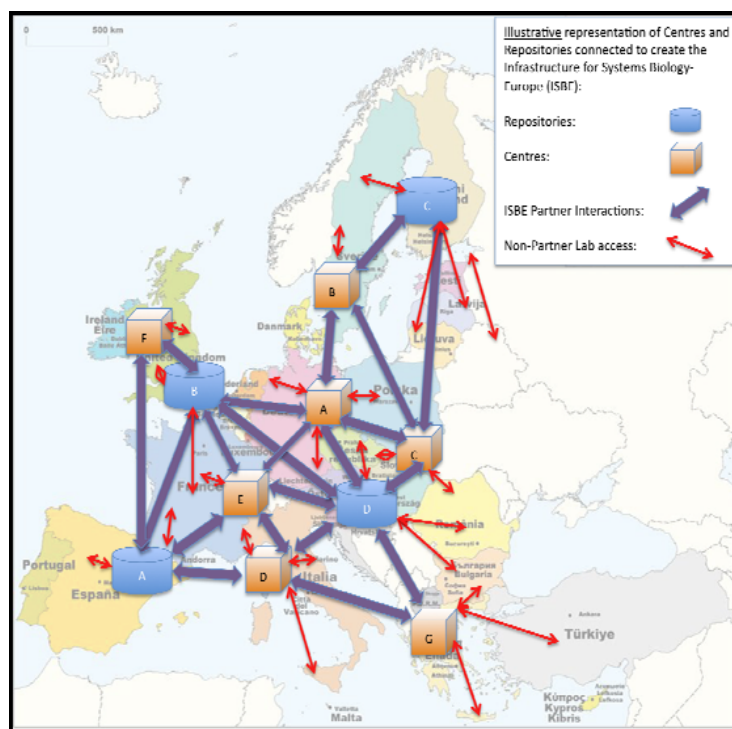
ISBE is envisaged as an infrastructure where clusters of research groups from institutions/centres will focus their various and specialised expertise on discovery-directed and hypothesis-driven research, and/or by contributing to the development of underpinning technologies. Some clusters will focus on distinct conceptual aspects of biology - such as model organisms, model cell populations, diseases, biotechnology, ecology etc.; others will have a central focus on the development and application of new technologies. The combined expertise and facilities of ISBE will serve the European Research Area by functioning as the entity for addressing important scientific problems, by disseminating technologies and by providing open and active access to data, software and experimental and modelling facilities (e.g. to the extent of enabling external researchers to perform experiments in a relevant cluster either directly or real-time-through-web). Although ISBE institutions/centres will have complementary activities, each will typically support the following: *de novo* data generation, data extraction from all pre-existing sources, data management and curation, data analysis, model extraction from literature, *de novo* model generation and validation, visualisation and modelling, dynamic interaction of models and data, model-driven experimental design, and

training. Importantly, ISBE will take a leading role in exploring, developing and establishing the necessary standards for experimentation and modelling in systems biology, critical for ensuring the delivery of reliable and consistent data across the infrastructure and beyond.

European science has the inherent ability to achieve these objectives in principle, but there is no infrastructure in place to integrate the fragmented effort that exists. A key deliverable of ISBE will be to bring focus to these disparate efforts by identifying, structuring and supporting large-scale research projects on major areas of urgent need in medicine, the biosciences and the economy - for example, human physiology and ageing, complex diseases, bioenergy and biomanufacturing. An ability to have a significant impact in these areas is currently beyond the capability of any single European institution. Coordination of effort through ISBE addresses not only this point, but also provides support to individual laboratories and smaller, medium size consortia that have succeeded in national or European grant applications. ISBE will be of particular benefit to less well-funded groups in the emerging economies of some Member States. Each individual laboratory will benefit from the step-change in the quality of science achievable through provision of an integrated infrastructure and the organisation and management which will ensure the continued development and sustainability of this infrastructure. This will be particularly true in relation to the new Member States of Eastern Europe. A robust, open, transparent and competitive process will be put in place to define the management and organisational structure and its membership. Finally, such a focused European infrastructure will offer a single point of contact for access to a network of best practice in systems biology, unique in the world, stimulating contacts with non-EU consortia from academia, industry and regulatory agencies across the globe, as well as other related infrastructures and programmes within the EU (for example the Innovative Medicines Initiative (IMI), Integrated BioBank of Luxembourg (IBBL), BBMRI, EATRIS, ECRIN, ELIXIR, EURO-Biolmaging, INFRAFRONTIER).

#### ***4. Technical Case: Summary of results (technical specifications) of conceptual and/or technical design studies.***

ISBE will integrate the elements of the European systems biology activity through a regulated infrastructure made up of (i) **HUBS**: scientific centres of excellence in systems biology, providing analytical technologies (e.g. proteomics, metabonomics, genomics, etc..) and/or computational biology, modelling and informatics; (ii) **Readily accessible REPOSITORIES**: for storing and archiving data and models, meeting the local HUB needs as well of those of the distributed network. The repositories will provide datasets which are not being provided by other infrastructure initiatives, but have been identified as required by them, e.g. physiological datasets, dynamic datasets, formal models (e.g. Bayesian, dynamical) and molecular networks. The new repositories would be structured to enable sample-specific access to data and to support systems biology approaches by linking structural and dynamic data. It is anticipated that these new databases would facilitate the medical and biological validation of models by researchers in EATRIS and BBMRI; (iii) **REAL-TIME CONNECTIONS**: between components within and between (i) and (ii), and with the systems biology research groups across Europe. The ISBE concept is thus to increase the efficiency of interaction between key systems biology practitioners and experts across the EU, thereby drawing expertise together with common purpose around specific complex tasks. High-speed, high-capacity, fit for purpose computer networks will enable real-time multidisciplinary experiments to be undertaken iteratively without teams being in the same location it is intended that these will be provided as part of the European academic broadband infrastructure (e.g. JANET in the UK) and/or by commercial telecommunications providers. Hence, an underlying feature of this proposal is that a broadband infrastructure will connect all the participants in ISBE. The ISBE e-infrastructure will reduce the need for physical interactions of scientists to complete research using these through-web facilities. As systems biology approaches begin to allow the modelling of entire organisms and ecosystems, models of their components will be run, managed and quality controlled at geographically distant sites (see Figure 33).



**Figure 33:** Centres and repositories connected to create the Infrastructure for Systems Biology – Europe (ISBE)

The standardisation of experimentation and modelling is a critical success factor for delivering not only the specific objectives of ISBE, but also those of systems biology in general. Standards are indispensable for data integration and will be the key to ensuring consistency across the distributed network of laboratories. Thus, the development of the necessary standards (whether reporting guidelines, data formats or ontologies, as well as standard analysis tools), their continued assessment in practice and modification in the light of technical developments or know-how within the infrastructure is a core element of the work programmes to be developed.

The diagram illustrates how ISBE will operate conceptually. The centres represent centres of scientific expertise. We envisage that in a particular area of systems biology there may well be a number of physical centres (e.g. universities) which have expertise – these will comprise a cluster of expertise which although geographically separated, will functionally comprise a cluster because they will be connected via the broadband network. Similarly, the data repositories for particular data types may be geographically separated, but will be linked via the high speed network.

**5. e-infrastructure: What does the new RI require as far as e-infrastructure? How is it integrated with the existing EU e-infrastructure (e.g. GÉANT, grid, digital repositories)?**

A fully functional ISBE will involve real-time remote experiments and modelling, and therefore will rely on high performance, high capacity networks (discussed in the previous section). ISBE will collaborate with GÉANT and its relevant national partners (e.g. JANET in the UK) to ensure that all ISBE participants are adequately connected. Additional high capacity networks will be required for some local sites and to link high-throughput experimental platforms. Similarly, the systems biology projects performed using ISBE will require high-performance computing both for large-scale data processing and for realistic multi-scale simulations. Collaborations between



ISBE, the European Grid Initiative (EGI) and its national partners will ensure the availability of large-scale distributed computing. For more demanding simulations, collaboration with Distributed European Infrastructure for Supercomputing Applications (DEISA) should provide access to the super-computing infrastructures of seven Member States. It is nevertheless anticipated that a lot of data (pre)-processing will have to be performed locally, and some ISBE centres will have their own computing clusters. The large amount of data required and generated by ISBE activities should be handled by or in collaboration with ELIXIR, and some ISBE centres may also be ELIXIR nodes. Local transitory and dedicated digital repositories not falling into ELIXIR's mission, but which will be needed will be handled by ISBE. In addition to existing EU e-Infrastructures, ISBE will require dedicated distributed computing tools and services. In particular, web-based experimentation and modelling will also require new robotic technology and newly trained human experts, as well as new software infrastructure (e.g. including workflows). An e-infrastructure on modelling and simulation, supporting the whole life cycle of model design, analysis, simulation and distribution shall link existing European partners into one ISBE functional cluster. The complete ISBE e-infrastructure (including the human capital involved) will therefore consist of: (a) the existing high-capacity network infrastructure, (b) new high performance connections to the individual sites of partners and experimental platforms, (c) software optimising the data and information transfer across the web, vis-à-vis the systems biology requirements, (d) software providing an interface between the web and biological equipment to include the deployment of robots to facilitate web-based experimentation, (e) programming of the robots themselves, (f) upgrading equipment in terms of its capabilities to interface rapidly with the information exchange systems, (g) the computation service personnel for the equipment, (h) computational systems biology experts at the hubs dedicated to the service functions of ISBE, (i) existing distributive supercomputing facilities for calculating entire organs, organisms and ecosystems and (j) dedicated computing facilities for ISBE specific highly-demanding tasks.

**6. Other expected socio-economic impacts: Development of new technologies, effects on training, involvement of industries, local impact, others.**

The beneficial impact of European Life Science research on society and industry needs to be and can be significantly enhanced. The complexity of living organisms, in terms of both the number of interacting components and the essential nonlinearities of the interactions, has limited the impact of current practice. Whereas science and technology has become extremely strong at the molecular level in living organisms, societal demand lies more at the level of entire functioning organs, organisms and ecosystems. Systems biology sits at the frontier of research in the Life Sciences, helping to translate the molecular detail into an understanding of how molecules interact dynamically to make such systems work, and is hence the missing link between the success of the molecular approaches and the areas where they might have greatest impact on society and industry. Systems biology is a highly interdisciplinary approach to the study of biological complexity in health and disease, biotechnology (including energy) and environmental science. ISBE stands a real chance of significantly increasing the quality and effectiveness of the science in areas such as health, green and white biotechnology, bio-energy and ecology, new health technologies and novel therapeutic interventions.

Over the past 20 years it has become clear that the understanding of how biological systems work is fundamental to the next phase of post-genome evolution in the Life Sciences. Single molecules may well contribute to life, but they are not, in themselves, alive. Medicine today needs to focus on the systematic diagnosis and treatment of complex diseases, but continues largely to practice the more traditional, single molecule, targeted approach, as currently this is all that is practicable. The availability of new systems biology infrastructures capable of supporting the reduction to practice and transfer of systems analytical technologies, and the translation of basic scientific discoveries into medicine and related areas, will improve our understanding of biology and living systems and contribute to the development of predictive, rather than empirical medical practice.

It will also enhance the economic potential of Europe by harnessing human resources and expertise more effectively in the development of new technologies and applications feeding into healthcare, pharmaceutical, agricultural and food industries. ISBE will provide an efficient test-bed for prototyping and evaluating relevant emerging technologies in partnership with others, and through the evolution of systems approaches will also create a process to help define user demand for further technical developments. This will be particularly true for engineering automatable experimental systems and the development of novel software tools. As such, these may represent opportunities for working with European industries or the creation of spin-out ventures themselves.

The network of centres of excellence in systems biology will offer increased opportunities for scientific exchanges within the infrastructure, broader connections to develop postgraduate and post-doctoral training in new approaches to multidisciplinary science. Important to this training will be the development of a common curriculum in this area. It is envisaged that training will be made available more broadly through the design and delivery of modular on-line training programmes accessible via the web. Much of this, as well as the broad day-to-day project engagement offered through the infrastructure, will be particularly important for research teams located in the less-well developed Member States within the EU, enabling them to contribute their knowledge and expertise and draw on that of others in the infrastructure in a way that would otherwise be impossible to the same scale. This will help to bridge the gap between Eastern and Western Europe and contribute to the development of a level playing field for pan-European research in systems biology.

**7. Commitments/maturity: Which states/organisations have demonstrated interest/commitment in supporting and/or funding the proposal?**

**Germany:** Forschungszentrum Juelich GmbH (FZJ), Federal Ministry of Education and Research (BMBF)

**Austria:** Federal Ministry of Science and Research (BMWF)

**Belgium:** National Fund for Scientific Research (FNRS)

**Finland:** Academy of Finland (AKA)

**France:** French National Centre for Scientific Research (CNRS), Agence Nationale de la Recherche (ANR), Ministère délégué à la recherche (MdR)

**Greece:** Academy of Athens, Biomedical Research Foundation

**Israel:** Israeli Science Foundation (ISF)

**Netherlands:** Netherlands Organisation for Scientific Research (NWO), Netherlands Council for Health and Development (ZonMw)

**Norway:** The Research Council of Norway (RCN)

**Slovenia:** Ministry of Higher Education, Science and Technology (MHEST)

**Spain:** Ministry of Science and Innovation (MICINN)

**United Kingdom:** Biotechnology and Biological Sciences Research Council (BBSRC)

**Italy:** Autonomous Province of Trento (PAT), Department of University and Scientific Research, Ministry of Education, University and Research (MIUR)

**Associated partners:**

**Luxembourg:** National Research Fund of Luxembourg (FNR)

**Switzerland:** Swiss National Science Foundation (SNF)

**8. Costs for construction, operation and decommissioning, indications on project financing. Give budget info in Mio €.**

Total preparatory cost	Total construction cost	Operation cost /year	Decommissioning cost
6 M€	300 M€	100 M€	Not applicable

**9. Timetable for construction, operation and decommissioning with duration and possible starting dates.**

Preparatory phase	Construction phase	Operation	Decommissioning
2010-2012	2012-2015	Starting 2015	

**10. Reference: Person who has submitted the proposal and will follow up in ESFRI.**

Professor Richard Kitney  
 Professor of BioMedical Systems Engineering  
 Imperial College London  
 South Kensington Campus  
 London SW7 2AZ  
 United Kingdom  
 Tel: +44 (0)20 7594 5184  
 Fax: +44 (0)20 7594 4297  
[r.kitney@imperial.ac.uk](mailto:r.kitney@imperial.ac.uk)



**1. Descriptive title and information on the ESFRI delegation submitting the proposal (or one of the members of EIROForum).**

**ANAE**  
**Infrastructure for Analysis and Experimentation on Ecosystems**  
 Submitted by the French ESFRI delegation

**2. Synthesis description of the new RI (or major upgrade) and S&T fields involved at pan-EU level in its use. Add links to relevant data/web pages.**

ANAE aims at developing a coordinated set of experimental platforms to analyse and predict the responses of ecosystems to environmental changes and to engineer management techniques that will allow buffering of and/or adaptation to these changes. This infrastructure will be instrumental for the implementation of forthcoming Joint Programming Initiatives in the field of environment such as the planned initiative „Agriculture, food security and climate change“.

The increasingly crucial environmental problems cannot be fully addressed with only an observational approach. ANAE will set-up a distributed and coordinated network of state of the art *in situ* and *in vitro* experimental platforms equipped with the latest instrumentation. They will be associated with analytical and modelling platforms and will be linked to networks of instrumented observation sites.

*In situ* long-term experimental platforms will be distributed across the main types of climate and land use (arable crops, grasslands, forest...). Major experimental treatments will refer to land management, climate and biodiversity and will be imposed for a long-term when needed. State variables of the system will be continuously measured in conjunction with the biogeochemical cycles, fluxes to hydrosphere and atmosphere and the dynamic of biodiversity. A few Ecotrons, highly instrumented, will allow deepening our understanding of processes and testing specific combinations of forcing variables. Enclosed in environmentally controlled chambers, ecosystems could be synthesized *de novo* or sampled in plots of the experimental platforms for a detailed analysis of the impact of long-term treatments. Analytical platforms at the cutting edge of technological development are needed to adapt the new investigation capacities to samples of soil, organisms or air and to help better understand and quantify the complex interactions between the different matter cycles, ecological states and compartments. Data base and modelling platforms will complete the infrastructure. A toolbox of numerical models will be developed to evaluate and predict the effects of climate and land use changes on ecosystem processes. Standardised data bases will ease establishing a library of model parameters for the range of ecosystems, climate and experimental conditions investigated. These data bases and models will allow linking ANAE to other European infrastructures in order to extrapolate the plot level experimentation to larger scales.

**3. Scientific Case: Scientific area(s) and potential and/or explicit users, how the new RI will fit into the existing and future landscape of research and of existing RIs, at EU and world level.**

In an era of dramatic changes in climate, land use and other human activities (Vitousek et al., 1997), understanding the responses of the biosphere to human drivers of environmental change is both an intellectual grand challenge and a practical necessity. Humans depend on a diverse set of ecosystem services like biomass production, including food, fibre, and fuel, and also depend on the maintenance of air and water quality (Millennium Ecosystem Assessment, 2005, Balmford & Bond Ecology Letters 2005). These services (provisioning, regulating and production) are strongly affected by human drivers and pressures of change such as climate change, land management, loss of biodiversity, air pollution, and water management (Marshall et al., 2008). Enhancements or disruptions, of these services by human-caused environmental

changes could alter the fundamental trajectory of the human endeavour over large parts of the world.

A wide range of biotic and physical processes links the biosphere to the geosphere, hydrosphere and atmosphere. Despite this link, our understanding of the biosphere does not match our increasingly sophisticated understanding of Earth's physical and chemical dynamics at regional, continental, and global scales (Williamson & Saros, 2008). Biospheric processes need to be studied in an integrated way with standardised, coherent experimental measurements for long periods of time (Schimel, 2007; Doney and Schimel, 2007). To date the existing monitoring observational programmes that collect data to meet regulatory, monitoring, and natural resource management objectives are not designed to address climate change and other new, complex, environmental challenges (Backlund et al., 2008). In fact, most of the existing networks observe either drivers of change (climate, land use) or a single or small number of response variables, but not drivers and responses in a coordinated analytical way. Rarely do environmental networks provide integrated observations of aspects of both pressures and impacts on the one side, and effects and responses on the other side, to allow a better and more holistic understanding of the underlying processes.

Moreover progress in environmental research was the result of disciplinary and reductionist attempts to analyze separate compartments of the environmental system. For example most environmental fluxes ( $N_2O$ ,  $CO_2$ , C sequestration...) have been studied separately from each other (disciplinary research) despite their strong interdependency (Chabbi and Lemaire, 2008). The residence time of the different elements (C, N, P...) within the different compartments of the ecosystem has not been well evaluated (Chabbi and Rumpel, 2009; Rumpel et al. 2009). As a consequence the majority of the current environmental problems cannot be clearly related to anthropogenic forcings despite large and costly research efforts.

Indeed, this approach (e.g. disciplinary and/or reductionist) was inevitable as a first step in our understanding of the complex hierarchical system. However, our comprehensive understanding of the full system, including the coupling and feedback mechanisms between all system components, depends on quite a different methodological approach directed at the large scale of the full system. This requires the availability of very large data sets and the multi-functional measurement and observation complementary platforms that measure, monitor and collect the data and materials necessary to study the dynamics of the state and fluxes within and between the compartments across a hierarchy of spatial and temporal scales.

To overcome the fragmentation of environmental and biodiversity research, it is necessary to develop **integrated experimental facilities** in Europe where (i) the relevant ecosystem processes will be analysed simultaneously, (ii) their coupling within ecosystem functions through cascades of interactions and feed-back loops will be studied, and (iii) the relation of ecosystem functions and services to biodiversity can be studied. These infrastructures must also provide **possibilities** to take into account ecosystem inertia and feedback-loops for accurate forecasting and to allow simultaneous measurements of key ecosystem variables and parameters through a multi-disciplinary approach (biogeochemistry, soil microbiology, atmospheric chemistry, hydrology, agronomy, forestry etc.).

Due to the various scales and the complexity of the interactions between ecosystem processes and the environmental conditions, meeting this challenge requires a sustained research effort with various approaches closely linked. Theoretical and mechanistic models, powerful „ecosystem analysers“ and long-term field experimentations are all needed to analyse, model and predict the consequences of global changes on biogeochemical fluxes and biodiversity. These tools need an integrated, innovative and concerted development across Europe. Such a development is the objective of the infrastructure for the Analysis and Experimentation on Ecosystems (ANAE). This infrastructure will allow the development of ecosystem science into modern systems biology using integrated and complementary approaches to generate and test hypotheses and to make predictions of ecosystems services under various future environmental and socio-economic scenarios.

**References:**

- Backlund, P., Janetos, A., Schimel, D., Hatfield, J., Ryan, M., Archer, S., & Lettenmaier, D. (2008). Introduction. In M. Walsh (Ed.), *The effects of climate change on agriculture, land resources, water resources, and biodiversity in the United States. Synthesis and Assessment Product 4.3* (pp. 11-20). Washington, DC: U.S. Environmental Protection Agency, Climate Change Science.
- Balmford, A; Bond, W. (2005). Trends in the state of nature and their implications for human well-being. *Ecology Letters*, 8, 1218-1234.
- Chabbi, A. & Lemaire G. (2008). Long term agro-ecosystem platforms for assessing biogeochemical cycles, environmental fluxes and biodiversity. In B. Christensen, J. Petersen & M. Schacht (Eds): *Long term field experiments – a unique research platform. Proceedings of NJF seminar 407. DJF Plant Science N° 137*, 73-75.
- Chabbi, A. & Rumpel, C. (2009). Organic matter dynamics in agro-ecosystems – the knowledge gaps. *European Journal of Soil Science*, 60, 153-157.
- Doney, SC; Schimel, DS (2007). Carbon and climate system coupling on timescales from the Precambrian to the anthropocene. *Annual Review of Environment and Resources*, 32, 31-66.
- Marshall, J., Blair, J., Peters, D. P. C., et al. (2008). Predicting and understanding ecosystem responses to climate change at continental scales. *Frontiers in Ecology and the Environment*, 6, 273-280.
- Millennium Ecosystem Assessment. (2005). *Ecosystems and human well-being: Synthesis*. Washington, DC: Island Press.
- Rumpel, C., Dignac, M.F., Chabbi, A. (2009). Molecular approaches to soil organic matter composition and dynamics. In R. Lal (Ed): *The Encyclopedia of Soil Science*, pp 24-30, Taylor and Francis Group.
- Schimel, D. (2007) Carbon cycle conundrums. *Proceedings of the National Academy of Sciences of the United States of America*, 104, 18353-18354.
- Vitousek, P. M., Mooney, H. A., Lubchenco, J., & Melillo, J. M. (1997). Human domination of Earth's ecosystems. *Science*, 277, 494-499.
- Williamson, C., Kratz, T., Dodds, W., et al. (2008). Lakes and streams as sentinels of environmental change in terrestrial and atmospheric processes. *Frontiers in Ecology and the Environment*, 6, 247-254.

**4. Technical Case: Summary of results (technical specifications) of conceptual and/or technical design studies.**

ANAE will provide **the scientific communities with complementary Research Infrastructures** to enable understanding and forecasting the impacts of climate change, land use change and biodiversity on continental ecosystem. To fulfil these overarching objectives, four types of complementary distributed platforms are necessary to experimentally submit ecosystems to the main forcing variables, to develop specific analytical methods and to provide databases and models:

§ **In situ long-term experimental platforms** will enable the manipulation of land management and/or climate parameters in a restricted number of ecosystem types and sites over long runs. State variables will be monitored in conjunction with the measurements of biogeochemical fluxes within soil and to atmosphere and hydrosphere and biodiversity dynamics. In terms of infrastructures and equipment, research institutions supporting these platforms will bring state of the art facilities, tools and methods, all of them complying to the following criteria: (i) long-term sites (data historicity), (ii) quality of the instruments and measuring methods and (iii) availability of open and user-friendly databases. **ANAEE will develop existing sites across a majority of European countries and will set up complementary ones where necessary.** A strong networking activity will coordinate the research activities, data management and access.

§ **Ecosystem analysers (Ecotrons)** will allow study of blocks of ecosystems of various sizes under a large array of controlled environments. State of the art instrumentation generally not available at the level of individual laboratories, will allow the measurements of a larger number of ecosystem processes and with a higher accuracy compared to the field. These measurements will provide new understanding of processes and will be highly suitable for calibration and intercomparison of models. Samples of ecosystems that have been treated by the *in situ* platforms over long periods of time will be analysed in the Ecotrons. New brief treatments, for example extreme events, can also be applied within the Ecotrons to study their interactions with the *in situ* treatments. **Ecotrons can be seen as ecological analysers receiving samples for analysis or as tools for models calibration.**

§ **Analytical platforms** will be developed to specifically analyse ecosystems components (soil, plants, water, microorganisms...). Elemental and molecular analysis will allow to identify and to track relevant chemical and biological markers of different ecosystem processes. Adaptations of generic analytical methods for the study of ecological processes are required. Structuring of analytical facilities regrouping high technology instrumentations and methodology expertises is necessary.

§ **In silico platforms** will be made up of a network of both existing and in-house simulation models and databases interconnecting with each other. Tight links with the experimental and analytical platforms will contribute strongly to the integration of knowledge and its dissemination to end users. Indeed, models developed and tested in Ecotrons and field scale experiments will be challenged against competing models and validated using data collected from environmental monitoring. **The information and knowledge gained from this research will also feed scenario simulations to evaluate environmental hazards and impacts on functional biodiversity resulting from a wide range of contrasting land use and management systems.**

#### ***5. e-infrastructure: What does the new RI require as far as e-infrastructure? How is it integrated with the existing EU e-infrastructure (e.g. GÉANT, grid, digital repositories)?***

ANAEE will provide data, models and simulations that will serve a variety of stakeholders' communities. To insure such crucial services, the quality, accessibility and interoperability of ANAEE outputs need to comply with the state of the art international standards and procedures. ANAEE will develop these standards and procedures in collaboration with developing international e-infrastructures:

##### ***- agreed quality standards***

Rigorous quality standards for data, metadata and ontologies, experimental protocols, and modelling procedures will be a prerequisite for ANAEE projects. A core of ecosystem variables collected according to common standards will be selected. Similarly, there will be an accreditation process for experimental and modelling procedures. ANAEE will to fully engage with the development of international standards. Adherence to these standards will be part of the quality management system that will be implemented within the ANAEE infrastructure.



**- ensure integrated data access and interoperability**

Access to ANAEE data will be provided using new tools that use international standard ontologies to retrieve data with particular properties, regardless of their location. ANAEE will contribute to the development of these ontologies to ensure they are fit for purpose, and allow access to ANAEE data by a range of environmental science disciplines and networks.

**- integrate experimentation and modelling**

ANAEE will integrate data acquisition and modelling in order to deliver high quality science that will support environmental policy. Data fed models are the vehicles for such transfer of knowledge. Indeed, ANAEE will impose a close collaboration between the communities of modellers, experimental and analytical scientists in order to establish scientific programmes that will be innovative, fit for purpose, and efficient in terms of resource use. Models will be developed, tested in Ecotrons and field scale experiments, challenged against competing models and validated using data collected from environmental monitoring. This dynamic way of working needs a modelling and informatics infrastructure that will foster innovation and will provide high quality policy relevant information.

**- links with developing international e-infrastructure**

Modelling toolboxes and interoperable metadata and data bases developed under ANAEE activities will feed and will take advantage of e-infrastructures developed in other projects, in particular LifeWatch and Integrated Carbon Observation System (ICOS). LifeWatch and ICOS will foster the dissemination of ANAEE to a large number of users and will provide additional tools to researchers (including ANAEE's teams) to further exploit the collected data. In this context ANAEE will develop data bases compliant to the Infrastructure for Spatial Information in Europe (INSPIRE) directive, the LifeWatch and ICOS reference model and the principles set for Global Earth Observation System of Systems (GEOSS) data sharing.

**- the infrastructure must be future-proof**

Ecosystem science is developing rapidly. Both data and models must be able to cope with such changes, including use of high resolution monitoring, environmental metabolomics etc., without losing continuity with historical data.

**6. Other expected socio-economic impacts: Development of new technologies, effects on training, involvement of industries, local impact, others.**

ANAEE, through the development of an integrated and multidisciplinary Research Infrastructure on terrestrial ecosystem, will have a strong impact in structuring the very fragmented research community (agronomists, soil scientists, ecologists, foresters, biogeochemists...) on terrestrial ecosystems around shared complementary infrastructures within the European Research Area. By the mean of promoting facilities for such an integrated approach, European Community would contribute at **boosting European research potential on continental biosphere at a high international level**. In this case ANAEE will be the "hard bone" of a strong development of integrated and inter-disciplinary research programmes on continental biosphere from the organisms to ecosystems, and from local processes to global changes. No nation in Europe has the capacity to develop alone such a programme of international scope.

Within the next ten years, the implementation of ANAEE research platforms as a distributed Research Infrastructure will place Europe among the world leaders in continental ecology science. Close contacts have to be developed with the USA related infrastructures (the highly instrumented monitoring network of infrastructures, National Ecological Observatory Network (NEON) and the Ecotron project Variable Atmospheric Laboratory (VAL)). Initial contacts have been taken during the course of the ANAEE design project. **It appears fundamental to joint the effort on the both sides of Atlantic for developing common standards and methodologies in prevision for a future worldwide integration.** The development of ANAEE infrastructures within emergent and non-developed countries is also a strategic issue, and the present ANAEE project should serve as springboard for such future development.

Another impact of the development of a like ANAEE network should be the opportunity to develop in Europe a strong **ecological engineering** approach in order to valorise all the expertise accumulated within this network in terms of manipulation or management of agro-ecosystem for optimising both their economic outputs and their ecological services. The long-term experimental platforms could be advantageously coupled sometime with more **operational monitoring and observations for environmental survey offering then unique research services to national or regional users** as environmental agencies, territorial management entities, national or regional parks etc.... Moreover, the modelling expertise and the data bases accumulated would provide unique tools for simulation of different prospective scenarios of land use and management of ecosystems at landscape level, and the evaluation of different environmental outputs. This would have also an impact on **teaching** agronomy, ecology and forestry with management perspectives by contributing to get a more holistic vision of the systems. This aspect should **attract young people to scientific education courses** by pointing out the strategic place of basic sciences for applications in terms of management decision for sustainable development.

#### **- Interactions with other EU programmes**

Strong collaborations with **LifeWatch** and **ICOS** programmes are envisaged. Two coordination meetings with these EU ESFRI initiatives, as well as with the NOHA and European Long-Term Ecosystem Research (LTER-Europe) networks, have been organised in 2009 by the ANAEE design project.

ANAEE will provide **LifeWatch** programme the requirements and user-cases allowing the construction of their "virtual" modelling labs such as information on responses of ecosystems and biodiversity to manipulated environmental variables within *in situ* and *ex situ* sites. This will be a significant complement to the analysis of the linkage between species and ecosystem level data gained through the analysis across sites planned in LifeWatch. LifeWatch will provide ANAEE with access to the construction planning in order to cooperate in creating dedicated "virtual modelling labs" for ANAEE user communities.

**ICOS** has for clear mission to provide long-term observations to quantify the greenhouse gas budget of Europe and adjacent regions. Indeed, a better link must be established between systematic flux-oriented observation networks (FLUXNET, etc...) and process studies such as the one that will be performed in the ANAEE platforms. In particular, operational ecosystem models that will assimilate ICOS data into time varying flux maps do need to be constrained by up-to date parameterisations and processes, relying upon ecosystem manipulative experiments and long-term datasets.

Conversely, "real world" observations of the climate response of fluxes provide guidance on a realistic domain of exploration that should be addressed by the design of controlled experiments, including future scenarios. In summary **ICOS** will provide ANAEE **with long-term permanent ecosystem monitoring at selected site across Europe** and **ANAEE will provide ICOS with additional and complementary long-term integrated facilities with manipulative experiments to analyse the ecosystem responses to forcing variables at process site-level.**

Indeed, all these infrastructures are complementary and address specific questions related to a specific part of the continental system. In addition they add value to each others operations, and thus provide the scientific user community with advanced services from their collective fabric of interrelated, but independent infrastructures.

#### **- Socio-economic issues**

The ANAEE infrastructure will not have capacity to develop socio-economic issues by its own. Nevertheless, the interactions developed between ANAEE and other EU programmes operating at larger scales could allow the accounting for socio-economic problems. So ANAEE should be integrated within a large cluster of EU programmes dealing with analysis of socio-economics impacts of ecosystems modifications through human activities, and elaboration of

environmental policies for restoration of ecosystem services. Interactions of ANAEE with LTER-Europe network and more precisely with LTER sites devoted to socio-economic impacts at regional scale should be a great opportunity for analysing trade-offs between ecosystem services and for developing integrated and sustainable development systems.

Furthermore, the development of the ANAEE complementary integrated experimental platforms will enable the European scientific community to enter large joint programmes aimed at tackling the major scientific and societal environmental issues. These issues imply the more integrated and multi-disciplinary approaches allowed by Joint Programming but they also require the support of targeted infrastructures.

### **7. Commitments/maturity: Which states/organisations have demonstrated interest/commitment in supporting and/or funding the proposal?**

ANAEE has been classified as **emerging infrastructure** within the ESFRI Roadmap in 2006. The ANAEE design study project founded by the EU Commission (2008-2009) allowed us to:

- (i) constitute an enlarged, well structured consortium of research teams ready to be actively involved in a structured network of research platforms and dedicated to raise their standards;
- (ii) establish a nucleus of national research institutions ready (see below) to support actively the emergence of such a distributed world level infrastructure;
- (iii) detail the specification of the different types of platforms, their costs and their as well as the administrative and legal status (e.g. ERIC) of the future infrastructure.

The significant progress made under the design study structured our scientific community and matured our infrastructure initiative to a level compatible with **starting an ESFRI Preparatory Phase**.

Taking advantage of the momentum of the design project and to get rapidly concrete and operational the enlarged consortium, lead by France, submitted an I3 proposal under the FP7 call "INFRA-2010-1.1.17: Sites and experimental platforms for long-term ecosystem research". The proposed project (EXPEER) via its ambitious programme of networking and joint research activities will set up a common framework and roadmap for improving the quality and performance of these platforms in a durable and sustainable manner.

Repeated contacts with research organisations and ministries representatives during the course of the design project raised their interest for developing new infrastructures under an ESFRI ANAEE initiative. While several of them will need additional discussions during a Preparatory Phase before deciding any funding, representatives of a few countries already included ANAEE infrastructures in their national roadmaps and planned future fundings.

France already started to fund through Institut National de Recherche Agronomique (INRA) large and heavily instrumented long-term experimental platforms for different ecosystems types: forest, grasslands and arable crops. Through CNRS, France also started to build an international Ecotron in Montpellier. The funding of a further implementation of this facility is planned under the national large infrastructures roadmap. Spain has also included the funding of a major *in situ* heavily instrumented platform (the Doñana reserve) in its national roadmap. Germany will continue the development of its TERrestrial ENvironmental Observatoria (TERENO) and the biodiversity-exploratories infrastructures. TERENO is a network of terrestrial observation and experimental platforms for the investigation of consequences of global change on the functioning of terrestrial ecosystems and the socioeconomic implications, while the biodiversities-exploratories addressed feed backs for realistic landscape scenarios at sufficient scales by combining monitoring with designed experiments and modelling. The National Academy of Science in Norway just decided to fund (2010-2011) a Preparatory Phase

for a future building of a national Ecotrons that would be shared by all the Norwegian institutes involved in environmental sciences, agronomy and ecology. The **perspectives of an ANAEE European infrastructure contributed to this decision**. Similarly, the active involvement of English researchers and funding agency representatives in ANAEE was instrumental in the decision of BBSRC to support the development of new ANAEE platforms within their agricultural stations. Food security is a key strategic driver for BBSRC and one of the main areas of research is in understanding how current knowledge of the individual basic components of agri-systems can be scaled up and applied to agricultural landscapes in order to increase food production in a more sustainable way.

**List of Research Institutions supporting the ANAEE project:**

INRA (France)  
 CNRS (France)  
 Technische Universität München, TUM (Germany)  
 Deutsches GeoForschungs Zentrum GFZ (Germany)  
 Forschungszentrum Jülich, FZJ (Germany)  
 Friedrich-Schiller-Universität Jena (Germany)  
 Geobotanik, Universität Freiburg (Germany)  
 Karlsruher Institut für Technologie, KIT (Germany)  
 Helmholtz-Zentrum für Umweltforschung GMBH, UFZ (Germany)  
 Rothamsted Research (UK)  
 Scottish Crop Research Institute, SCRI Scotland, (UK)  
 Imperial College of Science, Technology and Medicine (UK)  
 University of Southampton (UK)  
 Institute of Biological, Environmental and Rural Sciences (UK)  
 Natural Environment Research Council, NERC (UK)  
 Consiglio Nazionale delle Ricerche, CNR (Italy)  
 University of Napoli (Italy)  
 University of Padova (Italy)  
 Università degli Studi di Torino (Italy)  
 Institute for Natural Resources, CESIC, Seville (Spain)  
 Universiteit Antwerpen (Belgium)  
 Vereniging voor Christelijk Hoger Onderwijs, VUA (The Netherlands)  
 Bundesforschungs und Ausbildungszentrum für Wald, Naturgefahren und Landschaft (Austria)  
 Umweltbundesamt GMBH, EAA (Austria)  
 Danmarks Tekniske Universitet, DTU (Denmark)  
 Norwegian Institute for Agricultural and Environmental Research (Norway)  
 Kungliga Tekniska Högskolan, KTH (Sweden)  
 Lunds Universitet (Sweden)  
 Suomen Ympäristökeskus, SYKE (Finland)  
 Helsingin Yliopisto, UHEL (Finland)  
 Forschungsinstitut für Biologischen Landbau Stiftung, FIBL (Switzerland)  
 Eidgenössisches Volkswirtschaftsdepartement, EVD, (Switzerland)  
 Ústav systémové biologie a ekologie AV ČR, v.v.i., ISBE, (Czech Republic)  
 Europejskie Regionalne Centrum Ekohydrologii pod auspicjami UNESCO, (Poland)  
 MTA Ökológiai és Botanikai Kutatóintézet (Hungary)  
 Štátna lešy Tanapu (Slovakia)  
 Universitatea din Bucuresti (Romania)  
 Univerzitet u Novom Sadu (Serbia)  
 Ben Gurion University of the Negev BGU (Israel)

**8. Costs for construction, operation and decommissioning, indications on project financing. Give budget info in Mio €.**

The cost of construction of the different ANAEE Infrastructures will be more precisely estimated **during the Preparatory Phase** since each country will decide its specific level of investment in some or all components of ANAEE. The costs indicated below are only indicative.

Total preparatory cost	Total construction cost	Operation cost /year	Decommissioning cost
(of which already spent or committed)  <b>9 Mio €</b>	(specify contributions committed or indicated by possible funders)  <b>210 Mio €</b>  <b>ECOTRONS</b> <b>4x20 Mio € = 80 Mio €</b> <b>LTEPs 30x2 Mio € = 60 Mio €</b> <b>Analytical Platforms = 3x20 Mio € = 60 Mio €</b> <b>Eco-Modelling Platforms 10 Mio €</b>	(specify contributions by possible funders)  <b>12 Mio €</b>  <b>ECOTRONS 4 Mio €</b> <b>LTEPs 3 Mio €</b> <b>Analytical Platforms= 4 Mio €</b> <b>Modelling Platforms 1 Mio €</b>	(possible funders)

**9. Timetable for construction, operation and decommissioning with duration and possible starting dates.**

The preparatory phase <b>(2011 – 2014)</b> will develop the strategic plan for constructing the infrastructure, the funding commitments will be endorsed by stakeholders, and the initiative will be technically developed up to the level of a demonstration of full operation, but with a reduced numbers of sites.	The construction phase <b>(2012 – 2017)</b> may start at different dates in each country. This phase will complete the development of the infrastructure according to the strategic plan.	The operation phase <b>(2015 – 2035)</b> starting in 2015 and scheduled to last for 20 years, after the full scale deployment of the infrastructures, will run data collection in an operational mode. Ecosystem function and services will be determined and evaluated on a routine basis. Regular review process of assessment of the infrastructures performances will be established.	Decommissioning
---	---	---	-----------------

**10. Reference: Person who has submitted the proposal and will follow up in ESFRI.**

PhD Dr. HdR Abad CHABBI  
National scientific coordinator of the long-term observatories (ORE-ACBB)  
INRA Poitou-Charentes  
Route de Saintes BP 6  
86600 Lusignan  
France  
Tel. +33 (0) 5 49 55 61 78  
Tel. +33 (0) 5 49 55 60 24 (secrétariat)  
Mobil: +33 (0) 6 82 80 02 85  
Fax +33 (0) 5 49 55 60 66  
[abad.chabbi@lusignan.inra.fr](mailto:abad.chabbi@lusignan.inra.fr)

**1. Descriptive title and information on the ESFRI delegation submitting the proposal (or one of the members of EIROForum).**

**MIRRI**  
**Microbial Resource Research Infrastructure**  
Submitted by the French ESFRI delegation

**2. Synthesis description of the new RI (or major upgrade) and S&T fields involved at pan-EU level in its use. Add links to relevant data/web pages.**

MIRRI brings together European Microbial Resource Collections (MRC) with stakeholders (their users, policy makers, potential funders and the plethora of microbial research efforts) aiming at improving access to enhanced quality microbial resources in an appropriate legal framework, thus underpinning and driving Life Sciences research. It will build the European platform within the future Global Biological Resource Centre Network (GBRCN) for microorganisms.

Biological resources, such as microorganisms and their derivatives, are the essential raw material for the advancement of biotechnology, human health and research and development in the Life Sciences. The ESFRI Roadmap (2008) emphasises the evident need for improved availability of high quality materials and reagents for the study of species other than humans i.e. the animals, plants, bacteria - microorganisms. MIRRI cross cuts and supports most biotechnological sectors. It will help in the understanding of the role of microbial diversity in the area of soil fertility, food and agriculture, needed to develop approaches to improve agricultural and food production. Products derived from microorganisms include drugs, antimicrobials, biopesticides and industrial enzymes. Uses include biocontrol, biofuel production and direct use as food. Better managed resources will lead to further discovery in all areas of the Life Sciences including healthcare. MIRRI integrates services and resources, bridging the gap between the organism and provision of innovative solutions and products for green, grey and white biotechnology. MIRRI provides coherence in the application of quality standards, homogeneity in data storage and management and sharing the workload to help to release the hidden potential of microorganisms.

The Preparatory Phase focuses on governance and structure including technical, legal governance and financial issues. It establishes the links between the microbiological resource centre community, its users, policy makers and potential funders. It builds on:

- The foundation set by the OECD Biological Resource Centre (BRC) Task Force providing best practice<sup>1</sup>
- The GBRCN demonstration and the European Consortium of Microbial Resource Centres (EMbaRC) projects
- Voluntary scientifically based collection network activities, such as World Federation for Culture Collections (WFCC) and European Culture Collections' Organisation (ECCO)
- MIRRI enhances existing European MRCs linking them to third country partners extending globally.

<sup>1</sup>OECD Best Practice Guidelines for Biological Resource Centres

[http://www.oecd.org/document/36/0,3343,en\\_2649\\_34537\\_38777060\\_1\\_1\\_1\\_1,00.html](http://www.oecd.org/document/36/0,3343,en_2649_34537_38777060_1_1_1_1,00.html)

See [www.gbrcn.org](http://www.gbrcn.org); [www.embarc.eu](http://www.embarc.eu); [www.eccosite.org](http://www.eccosite.org); [www.wfcc.info](http://www.wfcc.info)

**3. Scientific Case: Scientific area(s) and potential and/or explicit users, how the new RI will fit into the existing and future landscape of research and of existing RIs, at EU and world level.**

MRCs are collections of laboratory held, living biological material that can be exploited for global research, cross cutting the agricultural, food, healthcare and biotechnological sectors providing a basis for a bioeconomy<sup>2</sup>. Biotechnology continues to offer a future beyond depletion of our natural resources. More and more natural resource alternatives are being found using cells as factories e.g. biofuels, drugs, nutraceuticals food and beverages. This has been stressed in the OECD work towards the establishment of a BRC Network<sup>2</sup> in providing a basis for the development of microbiological based industries and leading to economic development. MIRRI will be the European partner in the future GBRCN ([www.gbrcn.org](http://www.gbrcn.org)).

MIRRI will improve quality and add value to the biological materials available for research, providing a comprehensive coverage of organisms and associated data. It will provide improved services to identify and characterise newly discovered strains that will help drive biotechnological research and place Europe at the head of microbial based innovation and bioeconomy<sup>3</sup> development. BRCs need further enhancement to provide adequate support for research, innovation and discovery. Agriculture and food security are facing the important challenges of globalisation, consumer demands and environmental concerns. MIRRI will provide resources and information to help resolve problems, improve production and provide protective measures. The mega diversity countries are outside Europe and the envisioned globalisation of the network will provide to Europe facilitated access to the huge, mainly undiscovered resources. MIRRI efforts will be strongly linked to initiatives being undertaken currently e.g. in Brazil, China, Japan, Kenya and Russia.

Currently the service of access to biological materials and information is fragmented and there are large gaps in materials and support provided.

- 66% of the current MRCs are active partners in the world market of scientific, industrial and educational organisations by providing their biological material
- 69 % of the current MRCs also offer training and consulting services
- European MRCs represent 31% of all MRC in the world but this number is decreasing
- Europe needs to compete better
- 80% of the collections hold less than 700 strains, i.e. 52% of all resources preserved in MRCs are held in small collections with 1 – 14 employees i.e. integration into a strong infrastructure would reduce administrative burden and add professionalism

The number of taxonomists is diminishing and most currently practicing are approaching retirement age. Training new specialists and planning for the future will ensure continued access to this expertise needed to support new species discovery. Current databases of molecular data are incomplete and have erroneous data; coordinated action across the Research Infrastructure using authenticated strains will ensure our future ability to identify and utilise new species. Such services are essential, as, for example biosafety, biosecurity and quarantine control is based upon knowing the name of the microorganism so that it can be compared to the controlled organism or pathogen lists. There are a plethora of initiatives and projects not considering the fate of the resources developed and the information generated at great expense. MIRRI will strive to coordinate the output of such initiatives to protect investments by enhancing the capacity to store, add value to and deliver essential services.

MIRRI will complement ESFRI initiatives such as EMBRC (focussing on marine biodiversity, „blue“ biotechnology), BBMRI (focussing on primary material of human origin, „red“ biotechnology) and ERINHA (focussing on high pathogenic organisms) by focussing on green



and white/grey biotechnology sectors. These areas would cover food security in its largest sense as well as support for the agricultural and industrial biotechnology sector.

MIRRI will be the link between the collection community, users of microorganisms, policy makers and research programmes. The links with the users and stakeholders would be created in the Preparatory Phase. MIRRI will provide the framework to:

- enable MRC's to keep pace with advancing technology
- create a common operational framework based on international best practice criteria<sup>1</sup>
- bring together the fragmented services of access to materials and information
- harmonise identification, authentication and preservation processes, adding value to resources
- facilitate access to resources whilst meeting national regulatory controls and thus facilitating cross disciplinary efforts to discover and develop new products to provide world leading scientific and technological leaps for Europe.

<sup>2</sup>*Biological Resource Centres – Underpinning the Future of Life Sciences and Biotechnology*  
(<http://oecdpublications.gfi-nb.com/cgi-bin/oecdbookshop.storefront>)

<sup>3</sup> *The Bioeconomy to 2030: designing a policy agenda*. OECD Publications 2009

#### **4. Technical Case: Summary of results (technical specifications) of conceptual and/or technical design studies.**

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 e.g.: the project *European Consortium of Microbial Resources Centres* - EMbaRC (EU FP7, Research Infrastructures, INFRA-2008-1.1.2.9) - 8 MRCs in 7 countries; the Global Biological Resource Centre Network Demonstration Project emanating from an OECD Working Party on Biotechnology initiative presently supported by the German Ministry of Education and Research - 24 MRCs in 15 countries and the European Culture Collections' Organisation (ECCO) - 66 MRCs in 24 countries. MIRRI will ensure implementation of best practice, improve coverage and add value and information to bridge the gap to better utilisation. Currently such collections provide many services but these are fragmented. Enhanced services envisaged by MIRRI include:

- Supply of authentic control and reference strains, microbial DNA and RNA
- Identification of microorganisms by state of the art technologies
- Strain typing and authentication
- Characterisation of isolates
- Screening, providing lead natural products
- A range of testing and consultancy services for customers at accredited facilities
- Assistance in management of invasive species
- Improved production in crops and commodities
- Storage of strains for public access, safe and private deposit 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 of cell cultures

Training offered includes:

- Managing collections, handling organisms and their long-term preservation
- Bacteriology, Mycology, Systematic Virology
- Identification methods and strain typing by molecular and phenotypic tools
- Master and Ph.D. students
- Study visits and access to resources
- Operation and database building characterisation technologies
- Establishment and operation of patent International Depository Authority (IDA)
- Knowledge for development opportunities

MIRRI will involve the **Stakeholders** – the **Global Collection Community** (e.g. World Federation for Culture Collections, 560 collections in 68 countries), **Scientists**, Bioindustry Trade Associations, Pharmaceutical Industry, Biotechnology Industry, **Policy Makers**, **Governments** – Science underpinning policy, **International Organisations** involved in Healthcare, Agriculture, Environment, Development and the **General Public**.

Further information on networking collections can be found at <http://www.gbrcn.org>; <http://www.embarc.eu>; <http://www.eccosite.org>;

#### **5. e-infrastructure: What does the new RI require as far as e-infrastructure? How is it integrated with the existing EU e-infrastructure (e.g. GÉANT, grid, digital repositories)?**

MIRRI will require an overarching information system and tools to access the distributed MRC data bases and link this biological strain data to other relevant data sources. Most of the MRC data is currently stored in electronic catalogues, many online, but not connected. There is still grey literature, non-digitised or isolated data sets that need digitising and/or integrating. Industry standards for data validation and interoperability need to be implemented. Linking the resultant high quality reliable collection data to plant and animal host data, molecular, functional genomic and chemical data, ecosystem and taxonomic hierarchical data will create new landscapes of information that can be intelligently interrogated to provide innovative directions for research and enable delivery of added value products.

MIRRI requires the major components of e-infrastructures as described by the ESFRI Roadmap: it requires distributed grids whilst integrating genomic data may require high performance computing facilities and digital repositories. MIRRI provides the microbial resource data that needs to connect to other digital repositories; data in their various forms (from raw data to scientific publications). MIRRI will need to work with ESFRI e-infrastructure projects to see how it can interlink forming a fully integrated system and achieve the intended common approach. Of relevance would be the GÉANT network - a multi-gigabit pan-European data communications network, dedicated to research and education use. MIRRI requires ICT research networking and the distributed infrastructure needs standard connectivity based on internet protocols and end-to-end services on a large scale. The unprecedented large quantity of microbial molecular, ecosystem, taxonomic relationship, chemical and geographical data may require the adoption of the so-called “grid paradigm”, a revolutionary distributed environment for sharing computing and storage resources, allowing new methods of global collaborative research. DEISA, which interconnects the biggest high performance computing centres in Europe, to allow them to operate as a unique high performance computing resource for cutting edge simulation requirements and the Enabling GRIDs for E-science in Europe (EGEE) to integrate applications from many other scientific and industrial fields may also be relevant. Additionally MIRRI will link to Global Biodiversity Information Facility (GBIF) and observe other initiatives such as Europathogenomics, the Genomic Encyclopedia of Bacteria and Archaea (GEBA) project and its larger follow-up „GENOME“. To define this information system it will be required to work with initiatives such as ELIXIR - Upgrade of European Bioinformatics Infrastructure.

#### **6. Other expected socio-economic impacts: Development of new technologies, effects on training, involvement of industries, local impact, others.**

MIRRI will assist in disseminating best practice emerging from projects such as GBRCN and EMbaRC, enhancing efficiency by harmonisation of procedures. Implementation of sound collection management, improved preservation and authentication of organisms is essential to guarantee quality and safety in the various areas of application. Confidence and compliance in the prevention of misuse of dangerous organisms will be delivered by the introduction of a biosecurity code of practice, in line with EU and OECD initiatives. Creating high quality data and its combination with data from other fields will produce information landscapes, and

through modern, interactive tools allow new interpretations and innovation.

Appropriately equipped and staffed MRCs can serve as control points for access to a nation's living natural resources, support control of crop pathogens for sanitary and phytosanitary needs in relation to world trade and as centres to control access to dangerous pathogens maintaining biosecurity. They also contribute to basic inventories to monitor changes in biodiversity due to threats to ecosystems such as pollution, climate change and alien invasive species. MIRRI will coordinate activities, liaising with policy makers to establish the facilitating policy and necessary operational framework.

MIRRI will provide the authentic high quality resources that will enable Europe to make better use of its microbial diversity and contribute globally to answering the big questions of climate change, healthcare, food security and poverty alleviation. In the global scientific world it will help reconcile management of microbial resources with compliance to regulations. The evolution of the biotechnology industry and its application to agriculture, health, chemical or energy industries ultimately depends upon our ability to harness the potential of biodiversity and all it has to offer. The EU initiative for a knowledge-based bioeconomy and the recent OECD Report *The Bioeconomy to 2030: designing a policy agenda*<sup>3</sup> 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. MIRRI will facilitate the process of identifying possible products and solutions from microorganisms. It will enable economies of scale, the efficiency of sharing skills and technologies and the capacity to bridge gaps and focus activities without duplication of effort.

MIRRI will offer a wide range of expert services and several outputs will have social impact in several areas for example:

*Biopiracy:* Use of unlawfully acquired genetic resources is a serious concern often addressed as a north/south issue. Mechanisms for legitimate access and fair and equitable sharing of benefits will be implemented.

*Bioterrorism:* This extremely important and emotive issue needs addressing carefully and appropriately; MIRRI can help control access against misuse through implementation of best practice and a code of conduct.

*Employment:* The development of the infrastructure and improved delivery of materials and information into the bioeconomy will generate employment opportunities.

*Poverty eradication:* MIRRI will help establish MRCs in the countries of developing economies with outputs that impact on the livelihoods of local communities.

*International development:* MRCs can impact directly on development providing mechanisms to utilise biodiversity within country for the direct benefit of the local population. MIRRI can support in-country capacity building in human resource development, facility enhancement and implementation strategy.

Improved access to high quality and appropriate organisms from MIRRI can support key activities such as:

- Identifying the role of microorganisms in sustainable land management and water control systems
- Increasing food supply and reducing hunger through a reduction in losses due to pests and diseases
- Reduction of negative or improvement of beneficial microbial impact after natural or man made disasters
- Helping provide the resources for enhanced sanitary and phytosanitary procedures to put

in place the requirements of the WTO

- Supporting educational strategies in developing innovative training opportunities for microbiologists
- Supporting health programmes, as microbes will be the source of new drugs to combat major disease
- Identifying microbial products from natural resources to enter new markets
- Providing natural resources for energy production e.g. biofuels
- Capacity building in environmental issues including threatened habitats and species, linking *in situ* and *ex situ* conservation programmes – MRC development will provide the *ex situ* mechanism

### 7. Commitments/maturity: Which states/organisations have demonstrated interest/commitment in supporting and/or funding the proposal?

There is evidence from the Life Science community and policy makers that an infrastructure to coordinate access to microbiological materials, their associated information and services is required. This is exemplified by the European Commission project **European Consortium of Microbial Resources Centres -EMbaRC** (EU FP 7, Research Infrastructures, INFRA-2008-1.1.2.9: Biological Resources Centres (BRCs) for microorganisms, Grant agreement number: FP7- 228310) and the Global Biological Resource Centre Network Demonstration Project, emanating from an OECD Working Party on Biotechnology initiative, presently supported by the German Ministry of Science and Technology. Substantial investments have been made in Japan, China, Thailand, Taiwan and Brazil to establish BRCs. The European Culture Collections' Organisation (ECCO) representing 66 microbial resource centres in 24 European countries recognises the importance of structured linkage and coordination.

**List of Microbial Resource Collections expressing interest:** ECCO, \* EMbaRC, ‡ GBRCN, and ♦ French CRB Network

<p><b>ECCO members</b>  <b>ACBR</b> – Austrian Centre of Biological Resources and Applied Microbiology, Austria  <b>ATHUM</b>, Culture Collection of Fungi, University of Athens, Department of Biology, Greece  <b>BANGAL</b>, National Bank of Algae Germoplasm, Institute of Applied Algology (IAA), University of Las Palmas de Gran Canaria, Spain  <b>BCCM™/IHEM</b>, Scientific Institute of Public Health – Louis Pasteur, Mycology Section, Belgium  <b>* ‡ BCCM™/LMBP</b>, Plasmid collection, Department of Molecular Biology, Belgium  <b>* ‡ BCCM™/LMG</b>, Universiteit Gent, Laboratorium voor Microbiologie, Belgium  <b>* ‡ BCCM™/MUCL</b>, Mycotheque de l'Université Catholique de Louvain, Belgium</p>	<p><b>BPIC</b>, Collections of Phytopathogenic Fungi and Bacteria, Benaki Phytopathological Institute, Greece  <b>* ‡ CABI</b>, Genetic Resources Collection, UK  <b>CAPM</b>, Collection of Animal Pathogenic Microorganisms, Veterinary Research Institute, Czech Republic  <b>* ‡ CBS</b>, Centraalbureau voor Schimmelcultures, The Netherlands  <b>CCAP</b>, Culture Collection of Algae and Protozoa (freshwater), Dunstaffnage Marine Laboratory, UK  <b>CCF</b>, Culture Collection of Fungi, Charles University, Faculty of Science, Czech Republic  <b>CCM</b>, Czech Collection of Microorganisms, Masaryk University, Czech Republic  <b>CCUG</b>, Culture Collection University of Göteborg, Department of Clinical Bacteriology, Sweden</p>	<p><b>CCY</b>, Institute of Chemistry, Slovak Academy of Sciences, Slovakia  <b>* ‡ CECT</b>, Coleccion Espanola de Cultivos Tipo, Universidad de Valencia, Edificio de Investigacion, Spain  <b>CELMS</b> Collection of Environmental and Laboratory Microbial Strains, University of Tartu, Estonia  <b>CFBP</b>, Collection Française des Bactéries Phytopathogènes, INRA Unité de Pathologie Végétale et Phytobactériologie, France  <b>CNCTC</b>, Czech National Collection of Type Cultures, National Institut of Public Health, Czech Republic  <b>* ‡ CRBIP</b>, Centre de Ressources Biologiques de l'Institut Pasteur, Paris, France  <b>DBVPG</b>, Dipartimento di Biologia Vegetale, Sez. Microbiologia Applicata, Università di Perugia, Italy</p>
--	---	---

<p><b>ECCO continued</b></p> <p>‡ <b>DSMZ</b>, Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH, Germany</p> <p><b>ECACC</b>, European Collection of Cell Cultures, Centre for Applied Microbiology and Research, UK</p> <p><b>EX</b>, Microbial Culture Collection, University of Ljubljana, Biotechnical Faculty, Department of Biology, Slovenia</p> <p><b>FCUG</b>, Fungal Cultures University of Göteborg, Department of Systematic Botany, Sweden</p> <p><b>HNCMB</b>, Hungarian National Collection of Medical Bacteria, "B. Johar" National Center for Epidemiology, Hungary</p> <p><b>HÜKÜK</b>, Culture Collection of Animal Cells, Foot and Mouth Disease Institute, Turkey</p> <p><b>IBT</b>, Mycology Group, Department of Biotechnology, Technical University of Denmark, Denmark</p> <p><b>IAFB</b>, Collection of Industrial Microorganisms, Institute of Agricultural and Food Biotechnology (IAFB), Poland</p> <p><b>IBA</b>, Collection of Microorganisms Producing Antibiotics, Institute of Biotechnology and Antibiotics, Poland</p> <p>‡ <b>ICLC</b>, Interlab Cell Line Collection Biological bank and cell factory National Institute for Cancer Research Genoa, Italy</p> <p><b>IEGM</b>, Institute of Ecology and Genetics of Microorganisms, Ural Branch of the Russian Academy of Sciences, Russia</p> <p><b>IPPAS</b>, Collection of Microalgae of the Institute of Plant Physiology, Russian Academy of Sciences, Russia</p> <p><b>ITEM</b>, Culture Collection of Toxigenic Fungi and their Secondary Metabolites, Instituto Tossine e Micotossine da Parassiti Vegetali - CNR, Italy</p> <p><b>KOS</b>, Collection of Salmonella Microorganisms, Institute of Maritime and Tropical Medicine, National Salmonella Centre, Poland</p> <p><b>KÜKENS</b>, Centre for Culture Collections of Microorganisms, Istanbul Medical Faculty, Department of Microbiology and Clinical Microbiology, Turkey</p> <p><b>LCP</b>, Museum National</p>	<p><b>MSCL</b>, Microbial Strain Collection of Latvia, University of Latvia, Latvia</p> <p><b>MNHN</b>, Musée National d'Histoire Naturelle, Luxembourg</p> <p><b>MEAN</b>, Mycotheque Estacao Agronomica Nacional, Portugal</p> <p>*‡<b>MUM</b>, Micoteca da Universidade do Minho, Engenharia Biologica, Campus de Gualtar, Portugal</p> <p><b>MUT</b>, Mycotheca Universitatis Taurinensis, Italy</p> <p><b>MZKI</b>, Microbial Culture Collection, National Institute of Chemistry, Slovenia</p> <p><b>NBIMCC</b>, National Bank for Industrial Microorganisms and Cell Cultures, Bulgaria</p> <p><b>NCAIM</b>, National Collection of Agricultural and Industrial Microorganisms, Hungary</p> <p><b>NCB</b>, National Culture Bank, Università di Udine, Dip. Biologia Applicata Difesa Piante, Area Rizzi, Italy</p> <p><b>NCCB</b>, The Netherlands Culture Collection of Bacteria, The Netherlands</p> <p><b>NCIMB</b>, National Collection of Industrial, Food and Marine Bacteria Ltd., Scotland, UK</p> <p><b>NCPF</b>, National Collection of Pathogenic Fungi, Public Health Laboratory, UK</p> <p><b>NCPPB</b>, National Collection of Plant Pathogenic Bacteria, FERA, UK</p> <p><b>NCPV</b>, National Collection of Pathogenic Viruses, UK</p> <p><b>NCTC</b>, National Collection of Type Cultures, HPA, UK</p> <p><b>NCYC</b>, National Collection of Yeast Cultures, ReNo Ltd, c/o Institute of Food Research, UK</p> <p><b>NIVA</b>, Culture Collection of Algae, Norwegian Institute for Water Research, Norway</p> <p><b>PCM</b>, Polish Collection of Microorganisms, Polish Academy of Sciences, Poland</p> <p><b>PYCC</b>, Portuguese Yeast Culture Collection, SA Biotecnologia, Fac. Ciencias e Tecnologia/UNL, Portugal</p> <p><b>RCCC</b>, Russian Cell Culture Collection, The Central Bank - Institute of Cytology, Russian Academy of Sciences, Russia</p> <p><b>RSKK</b>, Refik Saydam National Type Culture Collection, Turkey</p>	<p><b>SRC CCM</b>, Collection of Cultures of Microorganisms, VECTOR - State Research Center of Virology and Biotechnology, Russia</p> <p><b>SVCK</b>, Institut f. Allgemeine Botanik, Universität Hamburg, Germany</p> <p><b>VKM</b>, All-Russian Collection of Microorganisms, Institute of Biochemistry and Physiology of Microorganisms, Russian Academy of Sciences, Russia</p> <p><b>VKPM</b>, Russian National Collection of Industrial Microorganisms, Russia</p> <p>‡ <b>VTT</b>, VTT Culture Collection, Finland</p> <p><b>* = EMbaRC partner</b></p> <p><b>‡ = GBRCN partner</b></p>
--	--	--

d'Histoire Naturelle, Laboratoire de Cryptogamie, France	<b>SAG</b> , Sammlung von Algenkulturen, Germany		
<p>♦ <b>French CRB Network</b> <b>Pôle de recherche clinique</b>, Dijon , France <b>CNRS</b>, Université Lyon 1, France <b>CNR Toxoplasmosse</b>, Limoges, France <b>CNR Leishmania</b>, Montpellier, France <b>* CIRM</b> : INRA Centre International de Ressources Microbiennes, France <b>Genosol</b>, Dijon, France <b>CNR de la toxoplasmosse</b>, Reims, France <b>Université de Pau et des Pays de l'Adour</b>, Pau, France</p> <p><b>* = EMbaRC partner</b> <b>‡ = GBRCN partner</b></p>	<p><b>Collections outside Europe - ‡ (GBRCN partners)</b> <b>JKUAT</b>, Jomo Kenyatta University of Agriculture and Technology, Institute for Biotechnology Research, Kenya Makerere University Kampala, Uganda <b>CCFC</b>, Canadian Collection of Fungal Cultures, Agriculture and Agri-Food, Canada <b>ACCC</b>, Agricultural Culture Collection of China, China <b>CGMCC</b>, China General Microorganisms Culture Collection, China <b>NBRC</b>, NITE Biological Resource Center, Japan <b>CBMAI</b>, Coleção Brasileira de Microorganismos de Ambiente e Indústria, UNICAMP, Brazil <b>CLIOC</b>, Coleção de Leishmania do Instituto Oswaldo Cruz, Brazil</p>	<p><b>Organisations- International</b> World Data Centre of Microorganisms (WDCM), Japan World Federation for Culture Collections (WFCC) OECD - Organisation FEMS - Federation of European Microbiological Societies IUMS - International Union of Microbiological Societies</p> <p><b>Organisations- national</b> CRIA, Brazil WGL - Wissenschaftsgemeinschaft Gottfried Wilhelm Leibniz, Germany</p> <p><b>Country support</b> Discussions are being held with ESFRI country representatives: Belgium Czech Republic Denmark Estonia Finland France Germany Italy Latvia Poland Portugal Spain The Netherlands UK</p>	
<b>8. Costs for construction, operation and decommissioning, indications on project financing. Give budget info in Mio €.</b>			
Total preparatory cost	Total construction cost	Operation cost /year	Decommissioning cost
<p><b>3 Mio €</b> •Formalising the secretariat •Bringing together the consortium to agree governance and infrastructure •Developing the programme of work •Negotiating the</p>	<p><b>190 Mio €</b> •Establishing the secretariat and legal entity •Establishing the data base •Linking with information providers •Preparing and delivering project proposals</p>	<p><b>10.5 Mio €</b> •Secretariat costs •Governance meetings to set strategy •Stakeholder meetings •Activities to be formulated into projects and separately funded •Human Resource training</p>	Nil

operational framework •Market studies •Pilot studies in some of the areas of work •Underpinning existing services  to be updated during Preparatory Phase	•Investment in partner facilities to implement best practice •Upgrading MRCs to enable a broader coverage of organisms and Services (€100million) •Establishment of Human Resource Development programmes to train in relevant skills such as taxonomy  to be updated during Preparatory Phase	Facility upgrade and development	
(of which already spent or committed)	(specify contributions committed or indicated by possible funders)	(specify contributions by possible funders)	(possible funders)
<b>9. Timetable for construction, operation and decommissioning with duration and possible starting dates.</b>			
Preparatory phase	Construction phase	Operation	Decommissioning
2 years Initiating 2010	3 years Completion 2015	ongoing	-
<b>10. Reference: Person who has submitted the proposal and will follow up in ESFRI.</b>			
MIRRI coordinator: GBRCN Secretariat Julius Kühn-Institut (JKI), Institut für Pflanzenernährung und Bodenkunde, Bundesallee 50, D-38116 Braunschweig Germany Email: <a href="mailto:d.smith@cabi.org">d.smith@cabi.org</a> Tel: +49 531 596 2298 Represented by David Smith (GBRCN Secretariat), Dagmar Fritze (GBRCN Secretariat) and Chantal Bizet (Institut Pasteur) [ <a href="mailto:chantal.bizet@pasteur.fr">chantal.bizet@pasteur.fr</a> ]			





## 6 LESSONS LEARNED

The ESFRI Forum asked the BMS TWG to advise ESFRI on possible improvements in the management and coordination of RIs (see mandate Chapter 1 “Executive Summary”). The recommendations of the BMS TWG presented here are twofold: for the BMS sector itself and, more generally, for the ESFRI progress.

### 6.1 Recommendations for the BMS sector

The BMS RIs provide a framework for Europe to tackle the Grand Challenges of our times.

Inclusion on the ESFRI Roadmap has brought these RIs into a networked, integrated, pan-European research arena. To fully embed these RIs within a functioning **ERIL** that will contribute to the European knowledge economy, these RIs require guidance on procedures and how to harmonise activities if this **ERIL** is to be realised.

Issues being repeatedly discussed at the BMS coordinators’ meetings include a need for guidance as to the legal structure, the exchange of best practises, how to apply for PP, how to interact thematically and technically, how to make best use of existing resources, and how to maximise synergy.

Both networking between the first generation RIs and integration of the second generation ones with the original RIs represent urgent needs.

These needs can only be met by a sustained BMS TWG activity in monitoring the process and supporting ESFRI in its incubator role wherever possible. The ESFRI Forum is therefore asked to put emphasis on mentoring of the RIs by the TWGs, composed of relevant delegates from the Member States. The benefits include securing direct contacts between Member States’ representatives and the RIs.

One outcome identified since the BMS Report 2008 was that RIs have considerably increased their joint activities. The BMS RIs showed a high interest in acting jointly in

order to, for example, increase their visibility on the European RI stage. For this purpose they repeatedly requested services of a neutral body to support coordination and to harmonise the respective efforts.

This coordinating role was often asked to be performed by the BMS TWG Chair, seen as having no vested interests in any of the RIs (see Chapter 4.8 “Common activities of BMS RIs”). Such a coordinating body, accepted by all RIs, however, needs a budget to guarantee sustainability.

Such a coordination body in a given field (at least the BMS) could also ease and accelerate the learning process of new RIs which enter the ESFRI Roadmap. This could speed up the implementation process considerably.

All BMS RIs recognised this need for common activities and therefore introduced a common pot solution to jointly finance events, publications and other matters. This solution so far is very small and was only possible due to the unbureaucratic support of EMBL. This small step should however form the nucleus to a future solution for all RIs of the BMS sector.

ESFRI should advise the Council of Research Ministers, which originally mandated ESFRI, that a legal personality, a budget and sustainability of ESFRI and its TWGs is badly needed to achieve the envisioned **ERIL**. The science community expects a permanent contact point to address its infrastructural needs.

### 6.2 Recommendations for ESFRI

One of ESFRI’s strict rules for new RI initiatives is that as long as there are two or more competing RI proposals, this fact is a clear proof of immaturity. However, to meet the Grand Challenges by filling the remaining gaps on the infrastructure landscape ESFRI should help infrastructure initiatives during all developmental stages by facilitating integration and achieving the demanded level of maturity.

This need for a proactive role of ESFRI and its TWGs may differ from one scientific area

to another. There is a clear need for such a proactive role in scientific communities which are rather young and not yet well organised for several tens of years. In some areas there are competing scientific communities, which would benefit from a neutral mediating body. A TWG acting as a neutral body could overcome that bottleneck and instruct in finding ways towards a common RI which fills an identified gap in the RI landscape.

The RI landscape is rapidly expanding due to the demand to answer the Grand Challenges. At its beginning, ESFRI followed a bottom-up approach. However, as more RIs entered the ESFRI Roadmap the more the need increased for an integration of individual RIs and better coordination of existing RIs with new initiatives. It is only in this manner that new scientific fields may be integrated into the ever changing **ERIL**.

The decision of ESFRI in March 2009 to launch another, strictly limited, call for proposals for new RIs (see Chapter 5 "Evaluation of new proposals") was discussed in length at the Forum meeting in Prague. Concern was expressed that the ESFRI Roadmap would be undermined by a large and constantly increasing number of RIs. There were arguments that new RIs should only be accepted as other older RIs stemming from the same scientific area of research leave the ESFRI Roadmap.

However, mere numbers of RIs do not represent budgetary implications nor do they indicate to what extent the Grand Challenges can and will be met. It is important to note that the BMS RIs have budgets which enable also smaller Member States to participate in a substantial manner.

Moreover, the distributed character of the BMS RIs favours a broad participation across Europe and, indeed beyond Europe. BMS RIs, therefore, go back to the core idea of ESFRI: greater joint research efforts can address research needs for the benefit of mankind.

The next two years will prove which RIs of the first generation will enter the construction phase and which will disappear from the ESFRI Roadmap. After the end of the Preparatory Phase, primarily funded by the European Commission, Member States have to show their commitments to RIs of interest. If no sustainable support can be found, the number of the RIs on the ESFRI Roadmap will diminish anyway.

As stated in the mandate of ESFRI, it is important that the Roadmap remains a living document updated at regular intervals. RIs which are realised shall leave the ESFRI Roadmap towards a "list of success stories" while others have to leave since no sufficient support could be organised. ESFRI should retain its openness to fill gaps which are identified by the TWGs in their respective scientific landscapes. Therefore the next update of the ESFRI Roadmap should again be open to all fields of science, in order to avoid any wrong labelling in responding to a call.

For the BMS TWG it is obvious that there are still RIs which are badly needed by European researchers for the competitiveness of Europe. Europe is dependent on its research. The European Research Area **ERA is dependent on ERIL**, the European Research Infrastructures Landscape.

## GLOSSARY

<b>ADMET</b>	Absorption, Distribution, Metabolism, Excretion, and Toxicity
<b>Agri-Net</b>	EU-funded agricultural portal
<b>AKA</b>	Academy of Finland
<b>ALM</b>	Advanced Light Microscopy
<b>ANAEE</b>	Infrastructure for Analysis and Experimentation on Ecosystems
<b>ANR</b>	Agence Nationale de la Recherche
<b>AS</b>	Associated State
<b>AWI</b>	Alfred Wegener Institute for Polar and Marine Research
<b>BAC</b>	Bacterial Artificial Chromosome
<b>BBMRI</b>	Biobanking and Biomolecular Resources Research Infrastructure
<b>BBSRC</b>	Biotechnology and Biological Sciences Research Council
<b>BESSY</b>	Berliner Elektronenspeicherring-Gesellschaft für Synchrotronstrahlung
<b>BIO3MASS</b>	Pollution effects on the sustainable use of Poplar as renewable resource
<b>BMBF</b>	Bundesministerium für Bildung und Forschung
<b>BMS TWG</b>	Biological and Medical Sciences Thematic Working Group
<b>BMWF</b>	Federal Ministry of Science and Research, Austria
<b>BRC</b>	Bioinformatics Research Centre
<b>BRC</b>	Biological Resource Centre
<b>BRIDGE</b>	Bioscience center for bridging laboratory with agro-ecosystem analysis for climate change adaptation research
<b>BSL4</b>	Biosafety Level 4
<b>CA</b>	Collaboration Action
<b>CABRI</b>	Common Access to Biological Resources and Information
<b>CARS</b>	Coherent Anti-strokes Raman Spectroscopy
<b>CCBI</b>	Czech Chemical Biology Initiative
<b>CCMAR</b>	Centro de Ciências do Mar
<b>CCP4</b>	Collaborative Computational Project Number 4
<b>CDC</b>	Centers for Disease Control and Prevention
<b>CEEC</b>	Central and Eastern European Countries
<b>CeMM</b>	Center for Molecular Medicine of the Austrian Academy of Sciences
<b>CERBM</b>	European Center of Research in Biology and Medicine
<b>CERM</b>	Centro di Risonanze Magnetiche
<b>CERN</b>	Conseil Européen pour la Recherche Nucléaire
<b>ChemBioNet</b>	Resource Network to Support Chem. Biology Research in Academia

<b>CIRMMP</b>	Consorzio Interuniversitario Risonanze Magnetiche di Metalloproteine Paramagnetiche
<b>CISI</b>	Centre of biomolecular Interdisciplinary Studies and Industrial Applications
<b>CNRS</b>	Centre National de la Recherche Scientifique
<b>CRC</b>	Clinical Research Centres
<b>CREST</b>	Comité de la recherche scientifique et technique
<b>CSIB</b>	Centres for Integrative Systems Biology
<b>CSIC</b>	Consejo Superior de Investigaciones Científicas
<b>CT</b>	Computed Tomography
<b>CTSA</b>	Clinical and Translational Science Awards
<b>CTU</b>	Clinical Trial Units
<b>DCBI</b>	Danish Chemical Biology Initiative
<b>DCL</b>	Dutch Compound Library
<b>DEISA</b>	Distributed European Infrastructure for Supercomputing Applications
<b>DESY</b>	Deutsches Elektronen-Synchrotron
<b>DFG</b>	Deutsche Forschungsgemeinschaft
<b>DG</b>	Directorate General
<b>DIAMOND</b>	Dipole And Multipole Output for the Nation at Daresbury (Light Source)
<b>DNA</b>	Desoxyribonucleic Acid
<b>DRIVER</b>	Digital Repository Infrastructure for European Research
<b>DTU</b>	Danmarks Tekniske Universitet (Technical University of Denmark)
<b>EABB</b>	European Animal BioBanking Infrastructure
<b>EATRIS</b>	European Advanced Translational Research Infrastructure in Medicine
<b>EBI</b>	European Bioinformatics Institute
<b>EBRCN</b>	European Biological Resource Centres Network
<b>EC</b>	European Commission
<b>ECBD</b>	European Chemical Biology Database
<b>ECCO</b>	European Culture Collections' Organisation
<b>ECDC</b>	European Centre for Disease Prevention and Control
<b>ECRIN</b>	European Clinical Research Infrastructures Network
<b>ECU</b>	European Currency Unit
<b>EG</b>	Expert Group
<b>EGE</b>	European Group on Ethics
<b>EGGE</b>	Enabling GRIDs for E-science in Europe
<b>EGI</b>	European Grid Initiative

<b>EHEA</b>	European Higher Education Area
<b>eHTPX</b>	e-science resource for high-throughput protein crystallography
<b>EIB</b>	European Investment Bank
<b>EIBIR</b>	European Institute for Biomedical Imaging Research
<b>e-IRG</b>	e-Infrastructure Reflection Group
<b>ELIXIR</b>	European Life-science Infrastructure for Biological Information
<b>ELMI</b>	European Light Microscopy Initiative
<b>ELSI</b>	Ethical, Legal and Societal Issues
<b>EM</b>	Electron Microscopy
<b>EMbarC</b>	European Consortium of Microbial Resource Centres
<b>EMBL</b>	European Molecular Biology Laboratory
<b>EMBRC</b>	European Marine Biological Resource Centre
<b>EMCSBI</b>	European Mediterranean Crop Systems Biology Institute
<b>EMERGENCE</b>	coordination action within the EU-NEST-Activities, (FP6 Pathfinder) in the field of Synthetic Biology
<b>EMMA</b>	European Mouse Mutant Archive
<b>EMRC</b>	European Medical Research Council
<b>EMTRAIN</b>	European Medicines Research Training Network
<b>ENBREC</b>	European Network of Bipolar Research Expert Centres
<b>ENCITE</b>	European Network for Cell Imaging and Tracking Expertise
<b>ENE TWG</b>	Energy Thematic Working Group
<b>ENIVD</b>	European Network for Diagnostics of "Imported" Viral Diseases
<b>ENV TWG</b>	Environmental Sciences Thematic Working Group
<b>EORTC</b>	European Organisation for Research and Treatment of Cancer
<b>EPFL</b>	École polytechnique fédérale de Lausanne
<b>ERA</b>	European Research Area
<b>ERAB</b>	European Research Advisory Board
<b>ERAC</b>	European Research Area Committee
<b>ERC</b>	European Research Council
<b>ERIC</b>	European Research Infrastructure Consortium
<b>ERIL</b>	European Research Infrastructures Landscape
<b>ERINHA</b>	European Research Infrastructure on Highly Pathogenic Agents
<b>ESF</b>	European Science Foundation
<b>ESFRI</b>	European Strategy Forum on Research Infrastructures
<b>ESRF</b>	European Synchrotron Radiation Facility
<b>ESSP</b>	Earth System Science Partnership
<b>ETIDE</b>	European Training for Infectious Disease Emergencies
<b>EU</b>	European Union

<b>EU-OPENSREEN</b>	European Infrastructure of Open Screening Platforms for Chemical Biology
<b>Euro-Biolmaging</b>	Research Infrastructure for Imaging Technologies in Biological and Biomedical Sciences
<b>EUR-OCEANS</b>	European Network of Excellence for Ocean Ecosystems Analysis
<b>EuroHORCs</b>	European Heads of Research Councils
<b>EURONET-P4/ ENP4Lab</b>	European Network of P4 laboratories
<b>Euro-QUAM</b>	European infrastructure for QUALity of chemical and biological Measurements
<b>EVICAB</b>	European Virtual Campus for Biomedical Engineering
<b>EXPEER</b>	Distributed Infrastructure for Experimentation in Ecosystem Research
<b>FIMM</b>	Institute for Molecular Medicine Finland
<b>FLUXNET</b>	global network of micrometeorological tower sites
<b>FMP</b>	Leibniz-Institut für Molekulare Pharmakologie
<b>FNR</b>	National Research Fund of Luxemburg
<b>FNRS</b>	National Fund for Scientific Research, Belgium
<b>FP(2/4/5/6/7)</b>	2 <sup>nd</sup> /4 <sup>th</sup> /5 <sup>th</sup> /6 <sup>th</sup> /7 <sup>th</sup> Framework Programme
<b>FZJ</b>	Forschungszentrum Juelich GmbH
<b>GBIF</b>	Global Biodiversity Information Facility
<b>GBRCN</b>	Global Biological Resource Centre Network
<b>GC-MS</b>	Gas Chromatography-Mass Spectrometry
<b>GEBA</b>	Genomic Encyclopedia of Bacteria and Archaea
<b>GEOSS</b>	Global Earth Observation System of Systems
<b>GLP</b>	Good Laboratory Practice
<b>HGF</b>	Helmholtz-Gemeinschaft Deutscher Forschungszentren e.V.
<b>HIV</b>	Human Immunodeficiency Virus
<b>HPLC-MS</b>	High Performance Liquid Chromatography -Mass Spectrometry
<b>hSERN</b>	human Sample Exchange Regulation Navigator
<b>HTS</b>	High Throughput Screening
<b>HZI</b>	Helmholtz-Zentrum für Infektionsforschung
<b>I(C)T</b>	Information (and Communications) Technology
<b>I3</b>	Integrated Infrastructure Initiative
<b>IAR</b>	Individual Assessment Report
<b>IBBL</b>	Integrated BioBank of Luxembourg
<b>ICGEB</b>	International Centre for Genetic Engineering and Biotechnology
<b>ICOS</b>	Integrated Carbon Observation System
<b>ICREL</b>	Impact on Clinical Research of European Legislation

<b>IGBMC</b>	Institute of Genetics and Molecular and Cellular Biology
<b>iGEM</b>	international Genetically Engineered Machine competition
<b>ILL</b>	Institute Laue-Langevin in Grenoble
<b>IMBG</b>	Institute of Marine Biology and Genetics
<b>IMG</b>	Institute of Molecular Genetics
<b>IMI</b>	Innovative Medicine Initiative
<b>IMPC</b>	International Mouse Phenotyping Consortium
<b>INFRAFRONTIER</b>	European Infrastructure for phenotyping and archiving of model mammalian genomes
<b>INRA</b>	Institut National de Recherche Agronomique
<b>INSPIRE</b>	Infrastructure for Spatial Information in Europe
<b>INSTRUCT</b>	Integrated Structural Biology Infrastructure
<b>IP</b>	Intellectual Property
<b>IRCCS</b>	Istituto Di Ricovero e Cura a Carattere Scientifico
<b>ISBE</b>	Infrastructure for Systems Biology-Europe
<b>ISF</b>	Israeli Science Foundation
<b>IZSLER</b>	Istituto Zooprofilattico Sperimentale Lombardia ed Emilia-Romagna
<b>JANET</b>	UK's education and research network
<b>JP(I)</b>	Joint Programming (Initiative)
<b>LifeWatch</b>	e-science and technology infrastructure for biodiversity data and observatories
<b>LIMS</b>	Laboratory Information Management System
<b>LTEP</b>	Long-term Experimental Platform
<b>LTER</b>	European Long-Term Ecosystem Research
<b>LUCIA</b>	Ligne Utilisée pour la Caractérisation par Imagerie et Absorption
<b>MarBEF</b>	Marine Biodiversity and Ecosystem Functioning
<b>MAX-lab</b>	National Electron Accelerator Laboratory for Synchrotron Radiation Research, Nuclear Physics and Accelerator Physics
<b>MDC</b>	Max-Delbrück Centrum für Molekulare Medizin
<b>MED.BANK</b>	Mediterranean Biological Resources Center
<b>MGE</b>	Marine Genomics Europe
<b>MHEST</b>	Ministry of Higher Education, Science and Technology (MHEST), Slovenia
<b>MIAPAR</b>	Minimum information about a protein affinity reagent
<b>MICINN</b>	Ministry of Science and Innovation, Spain
<b>MIRRI</b>	Microbial Resource Research Infrastructure
<b>MITOSYS</b>	quantitative imaging data in human cells by automated microscopy
<b>MIUR</b>	Ministry of Education, University and Research, Italy

<b>MLP</b>	Molecular Library Program
<b>MoU</b>	Memorandum of Understanding
<b>MRC</b>	Microbial Resource Collection
<b>MRI</b>	Magnetic Resonance Imaging
<b>MS</b>	Member State
<b>NCE</b>	New Chemical Entity
<b>NCSB</b>	The Netherlands Consortium for Systems Biology
<b>NEON</b>	National Ecological Observatory Network
<b>NIH</b>	National Institute of Health
<b>NKI</b>	Nederlands Kanker Instituut (Netherlands Cancer Institute)
<b>NMR</b>	Nuclear Magnetic Resonance
<b>NWO</b>	The Netherlands Organisation for Scientific Research
<b>OECD</b>	Organisation for Economic Co-operation and Development
<b>P<sup>3</sup>G</b>	Public Population Project in Genomics
<b>PC</b>	Programme Committee
<b>PCR</b>	Polymerase Chain Reaction
<b>PET</b>	Positron Emission Tomography
<b>PETRA</b>	Positron-Elektron-Tandem-Ring-Anlage
<b>PETs</b>	Privacy Enhancing Technologies
<b>PGRFA</b>	Plant Genetic Resources for Food and Agriculture
<b>PIMS</b>	Protein Information Management System
<b>PLACEBO</b>	PLatform Austria for ChEmical BiOlogy
<b>PP</b>	Preparatory Phase
<b>PRACE</b>	Partnership for Advanced Computing in Europe
<b>ProteomeBinders</b>	European infrastructure of ligand binding molecules against the human proteome
<b>PSE TWG</b>	Physical and Engineering Sciences Thematic Working Group
<b>PT-DLR</b>	Projektträger im Deutschen Luft- und Raumfahrtzentrum
<b>R&amp;D</b>	Research & Development
<b>R&amp;TD</b>	Research and Technology Development
<b>RCN</b>	Research Council of Norway
<b>RD&amp;D</b>	Research, Development & Demonstration
<b>RI</b>	Research Infrastructure
<b>RIVM</b>	National Institute for Public Health and the Environment
<b>RM</b>	Roadmap
<b>RNA</b>	Ribonucleic Acid
<b>RSFF</b>	Risk Sharing Finance Facility
<b>SARS</b>	Severe acute respiratory syndrome



<b>SAXS</b>	Small Angle X-ray Scattering
<b>SCAR (CWG)</b>	Standing Committee on Agricultural Research (Collaborative Working Group)
<b>SciColl</b>	Scientific Collections International
<b>SEAB</b>	Scientific and Ethical Advisory Board
<b>SERS</b>	Surface Enhanced Raman Spectroscopy
<b>SLS</b>	Swiss Light Source
<b>SME</b>	Small and Medium-Sized Enterprise
<b>SNF</b>	Swiss National Science Foundation
<b>SOP</b>	Standard Operating Procedures
<b>SPCT</b>	Single Photon Computed Tomography
<b>SPINE</b>	Structural Proteomics in Europe
<b>SPV</b>	Special Purpose Vehicle
<b>SSA</b>	Specific Support Action
<b>SSH TWG</b>	Social Sciences and Humanities Thematic Working Group
<b>STED</b>	Stimulated Emission Depletion
<b>SYNBIOSAFE</b>	Safety and Ethical Aspects of Synthetic Biology
<b>SystemsX.ch</b>	Swiss Initiative in Systems Biology
<b>SZN</b>	Stazione Zoologica „Anton Dohrn“, Naples
<b>TEEB11</b>	The Economics of Ecosystems and Biodiversity
<b>TERENO</b>	TERrestrial ENvironmental Observatoria
<b>TESSY</b>	Towards a European Strategy for Synthetic Biology
<b>ToR</b>	Terms of Reference
<b>VAL</b>	Variable Atmospheric Laboratory
<b>WFCC</b>	World Federation for Culture Collections
<b>WGE</b>	ESFRI Working Group on Evaluation
<b>WGL</b>	Wissenschaftsgemeinschaft Gottfried Wilhelm Leibniz e.V.
<b>WP</b>	Work Package
<b>XML</b>	eXtensible Markup Language
<b>XR</b>	X-ray diffraction
<b>YSBN</b>	Yeast Systems Biology Network
<b>ZonMw</b>	The Netherlands Organisation for Health Research and Development



# APPENDIX A LIST OF MEMBERS OF THE BMS TWG

(Status: 10/2010)

## Chair

**Eckhart Curtius**

## Secretariat

**Silke Gundel (since December 2009)**

**Ingrid Zwoch (July - December 2009)**

**Stefanie Zeretzke (till June 2009)**

**Marie-Christine Mahlke (since May 2007)**

Country	Name	Address
Austria	<b>Kurt Zatloukal</b>	Medical University Graz Auengruggenplatz 25 8036 Graz Austria <a href="mailto:kurt.zatloukal@meduni-graz.at">kurt.zatloukal@meduni-graz.at</a>
Belgium	<b>Pierre Hilson</b>	Functional Genomics VIB Department of Plant Systems Biology Ghent University Technologiepark 927 9052 Gent Belgium <a href="mailto:pihil@psb.vib-ugent.be">pihil@psb.vib-ugent.be</a>
Czech Republic	<b>Radislav Sedlacek</b>	Institute of Molecular Genetics AS CR, v. v. i. Department of Transgenic Models of Diseases Videnska 1083 142 20 Prague 4 Czech Republic <a href="mailto:radislav.sedlacek@img.cas.cz">radislav.sedlacek@img.cas.cz</a>
Cyprus	<b>Stavros Malas</b>	The Cyprus Institute of Neurology and Genetics 6, International Airport Avenue 1683 Nicosia Cyprus <a href="mailto:smalas@cing.ac.cy">smalas@cing.ac.cy</a>
Denmark	<b>Jørgen Frøkjær</b>	Clinical Physiology and Nuclear Medicine Skejby Sygehus Brendstrupgårdsvej 100 8200 Århus N Denmark <a href="mailto:jf@ki.au.dk">jf@ki.au.dk</a>

Country	Name	Address
EC Representative	<b>Jean-Emmanuel Faure</b>	European Commission Research Directorate General Research Infrastructures (Unit B3) Office SDME 1/133 1049 Brussels Belgium <a href="mailto:Jean-Emmanuel.Faure@ec.europa.eu">Jean-Emmanuel.Faure@ec.europa.eu</a>
Estonia	<b>Andres Metspalu</b>	The Estonian Genome Project of the Tartu University and Institute of Molecular and Cell Biology 23 Riia St. Tartu 51010 Estonia <a href="mailto:Andres@ebc.ee">Andres@ebc.ee</a>
Finland	<b>Taina Pihlajaniemi</b>	University of Oulu Biocenter Oulu PO Box 5000 90014 Finland <a href="mailto:taina.pihlajaniemi@oulu.fi">taina.pihlajaniemi@oulu.fi</a>
France	<b>André Syrota</b>	INSERM 101 rue de Tolbiac 75654 Paris France <a href="mailto:andre.syrota@inserm.fr">andre.syrota@inserm.fr</a>
Germany	<b>Ingrid Zwoch</b>	PT-DLR National Contact Point Life Sciences Heinrich-Konen-Str. 1 53227 Bonn Germany <a href="mailto:Ingrid.Zwoch@dlr.de">Ingrid.Zwoch@dlr.de</a>
Greece	<b>Dimitrios Thanos</b>	Biomedical Research Foundation Academy of Athens 4 Soranou Efessiou Street Athens, 11527 Greece <a href="mailto:thanos@bioacademy.gr">thanos@bioacademy.gr</a>
Hungary	<b>Gabor Szabo</b>	Institute of Experimental Medicine 120083 Budapest Szigony u. 43, Hungary <a href="mailto:szabog@koki.hu">szabog@koki.hu</a>

Country	Name	Address
Iceland	<b>Hakon Gudbjartsson</b>	VP Informatics, decode Genetics Inc. Strulugata 8, 101 Reykjavik Iceland <a href="mailto:hakon.gudbjartsson@decode.is">hakon.gudbjartsson@decode.is</a>
Ireland	<b>Ann Hever</b>	Health Research Board 73 Lower Baggot Street Dublin 2 Ireland <a href="mailto:AHever@hrb.ie">AHever@hrb.ie</a>
Israel	<b>Joel Sussman</b>	Weizmann Institute of Science Rehovot 76100 Israel <a href="mailto:joel.sussman@weizmann.ac.il">joel.sussman@weizmann.ac.il</a>
Italy	<b>Silvano Riva</b>	IGM-CNR Via Abbiategrasso 22007 27100 Pavia Italy <a href="mailto:riva@igm.cnr.it">riva@igm.cnr.it</a>
Lithuania	<b>Gintaras Valincius</b>	Institute of Biochemistry Mokslininku 12 LT 2008662 Vilnius Lithuania <a href="mailto:gintaras@bchi.lt">gintaras@bchi.lt</a>
Malta	<b>Brian St. John</b>	Malta Information Technology & Training Services Ltd. Gattard House National Road Blata-I- Bajda HMR 02 Malta <a href="mailto:Brian.st.-john@gov.mt">Brian.st.-john@gov.mt</a>
Netherlands	<b>Edvard Beem</b>	The Netherlands Organisation for Health Research and Development (ZonMw) P.O. Box 93245 2509 AE The Hague Netherlands <a href="mailto:beem@zonmw.nl">beem@zonmw.nl</a>
Norway	<b>Stig. W. Omholt</b>	Centre for Integrative Genetics Norwegian University of Life Sciences P.O. Box 5003 1432 Ås Norway <a href="mailto:stig.omholt@umb.no">stig.omholt@umb.no</a>

Country	Name	Address
Poland	<b>Wojciech Froncisz</b>	Jagiellonian University Cracow Faculty of Biochemistry, Biophysics and Biotechnology Gronostajowa 7 30 – 327 Krakow Poland <a href="mailto:wojciech.froncisz@uj.edu.pl">wojciech.froncisz@uj.edu.pl</a>
Portugal	<b>Ester Serrão</b>	Faculdade de Ciências do Mar e Ambiente Universidade do Algarve Campus de Gambelas 8005-139 Faro Portugal <a href="mailto:eserrao@ualg.pt">eserrao@ualg.pt</a>
Romania	<b>Gabriel-Lucian Radu</b>	Politehnica University of Bucharest Dept. of Analytical Chemistry and Instrumental Analysis 313, Spl. Independentei Bucharest Romania <a href="mailto:gl_radu@dbio.ro">gl_radu@dbio.ro</a>
Slovenia	<b>Irena Mlinarič-Raščan</b>	Faculty of Pharmacy, University of Ljubljana Askerceva 7, 100 Ljubljana Slovenia <a href="mailto:irena.mlinaric@ffa.uni-lj.si">irena.mlinaric@ffa.uni-lj.si</a>
Spain	<b>José López Carrascosa</b>	CNB – CSIC Campus de la Universidad Autónoma de Madrid Cantoblanco, 28049 Madrid Spain <a href="mailto:jlcarras@cnb.uam.es">jlcarras@cnb.uam.es</a>
Sweden	<b>Dick Heinegård</b>	Lund University Department of Clinical Sciences BMC plan C12 22184 Lund Sweden <a href="mailto:Dick.Heinegard@med.lu.se">Dick.Heinegard@med.lu.se</a>
Switzerland	<b>Michael Hengartner</b>	University of Zuerich Institute of Molecular Biology Winterthurerstrasse 190 8057 Zuerich Switzerland <a href="mailto:Michael.hengartner@molbio.uzh.ch">Michael.hengartner@molbio.uzh.ch</a>

Country	Name	Address
Turkey	<b>Murat Özgören</b>	Department of Biophysics Brain Dynamics Research Center Faculty of Medicine Dokuz Eylül University Balcova 35340 Izmir Turkey <a href="mailto:murat.ozgoren@deu.edu.tr">murat.ozgoren@deu.edu.tr</a>
United Kingdom	<b>Gabriela Pastori</b>	Biotechnology and Biological Sciences Research Council BBSRC Polaris House North Star Avenue Swindon, Wiltshire SN2 1UH United Kingdom <a href="mailto:gabriela.pastori@bbsrc.ac.uk">gabriela.pastori@bbsrc.ac.uk</a>

Function	Name	Address
Chair	<b>Eckhart Curtius</b>	Federal Ministry of Education and Research Unit 611 Life Sciences – Strategy and Policy Issues 53175 Bonn Germany <a href="mailto:Eckhart.Curtius@bmbf.bund.de">Eckhart.Curtius@bmbf.bund.de</a>
BMS Secretariat	<b>Silke Gundel</b> (since December 2009)	PT-DLR National Contact Point Life Sciences Heinrich-Konen-Strasse 1 53227 Bonn Germany <a href="mailto:Silke.Gundel@dlr.de">Silke.Gundel@dlr.de</a>
BMS Secretariat	<b>Ingrid Zwoch</b> (July - December 2009)	PT-DLR National Contact Point Life Sciences Heinrich-Konen-Strasse 1 53227 Bonn Germany <a href="mailto:Ingrid.Zwoch@dlr.de">Ingrid.Zwoch@dlr.de</a>
BMS Secretariat	<b>Stefanie Zeretzke</b> (till June 2009)	PT-DLR National Contact Point Life Sciences Heinrich-Konen-Strasse 1 53227 Bonn Germany <a href="mailto:Stefanie.Zeretzke@dlr.de">Stefanie.Zeretzke@dlr.de</a>
BMS Secretariat	<b>Marie-Christine Mahlke</b>	PT-DLR National Contact Point Life Sciences Heinrich-Konen-Strasse 1 53227 Bonn <a href="mailto:Marie-Christine.Mahlke@dlr.de">Marie-Christine.Mahlke@dlr.de</a>



## APPENDIX B SUMMARY OF THE MEETINGS

In the frame of the preparation of the ESFRI Roadmap 2010 the BMS TWG met seven times in 2009 and 2010. The main issue focussed on the preparation of the BMS Report which should represent on the one hand the actual situation of the ESFRI BMS RIs already on the Roadmap and on the other hand the future RIs to be included into the update of the ESFRI Roadmap 2010 on the basis of the scientific landscape in the Biological and Medical Sciences. In the following list the meetings and their specific purposes are shown. In addition to the regular BMS TWG meetings, a consensus meeting of the Expert Groups occurred at which the evaluation of the proposals took place.

A password protected working platform was created by the BMS TWG secretariat and provided to the BMS TWG members in November 2007. This platform contains all documents that were generated by the BMS Group (e.g. agendas and minutes of the meetings, proposals to be evaluated, assessment forms and guidelines, etc.) and was managed by the BMS TWG secretariat. With respect to ensure clarity and lucidity of the procedure, all BMS TWG members gained restricted access to the working platform.

Date	Title	Purpose
24 <sup>th</sup> / 25 <sup>th</sup> June, 2009	1 <sup>st</sup> BMS TWG / 3 <sup>rd</sup> Coordinators Meeting, Brussels	<ul style="list-style-type: none"> <li>Defining the role of the new BMS TWG</li> <li>Fulfilling the incubator role for all proposals</li> </ul>
19 <sup>th</sup> / 20 <sup>th</sup> October, 2009	2 <sup>nd</sup> BMS TWG / 4 <sup>th</sup> Coordinators Meeting, Hinxton	<ul style="list-style-type: none"> <li>Implementing the role of the new BMS TWG</li> <li>Fulfilling the incubator role for all proposals</li> <li>Drafting Group; Landscape</li> </ul>
09 <sup>th</sup> December, 2009	3 <sup>rd</sup> BMS TWG / 5 <sup>th</sup> Coordinators Meeting, Stockholm	<ul style="list-style-type: none"> <li>Exchange of best practice between the 10 BMS initiatives</li> <li>Involvement of the BMS Coordinators into the BMS Report</li> <li>Preparing the evaluation procedure for the update of the ESFRI Roadmap 2010</li> <li>Preparing the BMS Report 2010; creation of Drafting Groups</li> </ul>
10 <sup>th</sup> / 11 <sup>th</sup> March, 2010	4 <sup>th</sup> BMS TWG / 6 <sup>th</sup> Coordinators Meeting, Vienna	<ul style="list-style-type: none"> <li>Preparation of the BMS Report 2010</li> <li>Recent developments of RIs after PP</li> <li>Evaluation process of proposals for updated ESFRI Roadmap 2010</li> </ul>
08 <sup>th</sup> April, 2010	ESFRI BMS Consensus Meeting, Bonn	<ul style="list-style-type: none"> <li>Discussion of the BMS proposals for the update of the ESFRI Roadmap / BMS Report 2010</li> <li>Mutually agreed recommendations to the BMS TWG</li> </ul>

Date	Title	Purpose
16 <sup>th</sup> / 17 <sup>th</sup> June, 2010	5 <sup>th</sup> BMS TWG Meeting, Paris	<ul style="list-style-type: none"> <li>• Decision on the evaluation of proposals for the updated ESFRI Roadmap 2010</li> <li>• Preparation of the BMS Report 2010 (Input of the Drafting Groups)</li> </ul>
06 <sup>th</sup> / 07 <sup>th</sup> July, 2010	6 <sup>th</sup> BMS TWG / 7 <sup>th</sup> Coordinators Meeting, Oslo	<ul style="list-style-type: none"> <li>• Preparation of the BMS Report 2010</li> <li>• Recent developments of RIs</li> <li>• Update “Strategy Paper”</li> </ul>
13 <sup>th</sup> / 14 <sup>th</sup> September, 2010	7 <sup>th</sup> BMS TWG / 8 <sup>th</sup> Coordinators Meeting, Naples	<ul style="list-style-type: none"> <li>• BMS Report 2010 – state of the art and final approval</li> <li>• Strategy Paper of BMS RIs – Contents, Process, Meeting(s)</li> <li>• ERIC – Recent developments</li> </ul>

## APPENDIX C MEETINGS AND EVENTS OF THE BMS RIs

### Meetings and events of the six BMS Research Infrastructures of the first generation

BBMRI	
Date	Title
23 <sup>th</sup> – 24 <sup>th</sup> March, 2009	WP meetings and SEAB meeting
25 <sup>th</sup> – 27 <sup>th</sup> March, 2009	PHOEBE-P <sup>3</sup> G-BBMRI joint Conference
20 <sup>th</sup> March, 2009	1 <sup>st</sup> Stakeholder Forum
25 <sup>th</sup> March, 2009	BBMRI 2nd Governance Council Meeting
16 <sup>th</sup> September, 2009	Stakeholder Forum Discussion / Information Meeting
11 <sup>th</sup> November, 2009	Prototype Meeting
15 <sup>th</sup> December, 2009	Stakeholder Forum Patient Working Group Meeting
16 <sup>th</sup> December, 2009	Expert Center Meeting
03 <sup>rd</sup> January, 2010	Nature Meeting
09 <sup>th</sup> April, 2010	BBMRI meets Mediterranean Biobanks
09 <sup>th</sup> June, 2010	2 <sup>nd</sup> Stakeholder Forum
23 <sup>rd</sup> – 25 <sup>th</sup> September, 2010	Biobanking for Science Conference
29 <sup>th</sup> – 30 <sup>th</sup> November, 2010	Pilot-Phase human OECD GBRCN

EATRIS	
Date	Title
February, 2009	Governmental Partner Meeting
May, 2009	Decision on Implementation Phase from January, 2011 onwards
October, 2010	EATRIS Stakeholder Meeting, Basel
November, 2010	Publication Draft Business Plan
December, 2009	Annual Meeting
March, 2010	Establishment of process to create EATRIS as legal entity
June, 2010	Adoption of Memorandum of Understanding
August, 2010	Entry into Force of Memorandum of Understanding
September, 2010	Round Table Discussion "Open Innovation" at MipTec, 2010
October, 2010	Selection of EATRIS Host country
October, 2010	EATRIS Conference Rome: From Basic Research to Medical Innovation
November, 2010	Adoption of Implementation Agreement
November, 2010	Annual Meeting
December, 2010	Publication Final Business Plan

ECRIN	
Date	Title
07 <sup>th</sup> January, 2009	Project Development Board Meeting
20 <sup>th</sup> May, 2009	ECRIN annual meeting
September, 2009	Summer school (training of the European Correspondents)
19 <sup>th</sup> September, 2009	Decision voted by the Network Committee to apply to ERIC status
24 <sup>th</sup> November, 2009	Project Development Board meeting
25 <sup>th</sup> January, 2010	Decision voted by the Network Committee to include Poland as new partner
02 <sup>nd</sup> March, 2010	Project Development Board meeting
20 <sup>th</sup> May, 2010	Annual Meeting
21 <sup>st</sup> June, 2010	Users' meeting

ELIXIR	
Date	Title
26 <sup>th</sup> – 27 <sup>th</sup> March, 2009	5 <sup>th</sup> Steering Committee Meeting
19 <sup>th</sup> May, 2009	6 <sup>th</sup> Steering Committee Meeting
19 <sup>th</sup> – 20 <sup>th</sup> May, 2009	3 <sup>rd</sup> Stakeholders Meeting
22 <sup>nd</sup> – 23 <sup>rd</sup> October, 2009	7 <sup>th</sup> Steering Committee Meeting
22 <sup>nd</sup> – 23 <sup>rd</sup> July, 2010	8 <sup>th</sup> Steering Committee Meeting

INFRAFRONTIER	
Date	Title
20 <sup>th</sup> – 21 <sup>st</sup> April, 2009	INFRAFRONTIER Annual Meeting
01 <sup>st</sup> October, 2009	Start of European Medicines Research Training Network (EMTRAIN) with the other first generation BMS Research Infrastructures and pharmaceutical industry
16 <sup>th</sup> October, 2009	INFRAFRONTIER Scientific Strategy Meeting
11 <sup>th</sup> December, 2009	6 new partners from Czech Republic, Austria and Canada, Italy and France, including 3 new funding partners
14 <sup>th</sup> May, 2010	Circulation of draft Implementation Documents for INFRAFRONTIER Research Infrastructure
10 <sup>th</sup> June, 2010	INFRAFRONTIER Annual Meeting with discussion of Implementation Documents
September / October, 2010	Funders Meeting and Establishment of Inter-Ministry Working Group

INSTRUCT	
Date	Title
20 <sup>th</sup> January, 2009	Management Committee Meeting
27 <sup>th</sup> March, 2009	Management Committee Meeting
April, 2009	Annual Meeting
21 <sup>st</sup> May, 2009	Management Committee Meeting
23 <sup>rd</sup> May, 2009	Training event
22 <sup>nd</sup> June, 2009	Training event
22 <sup>nd</sup> November, 2009	Training event
26 <sup>th</sup> November, 2009	Management Committee Meeting
13 <sup>th</sup> January, 2010	Training event
20 <sup>th</sup> January, 2010	Management Committee Meeting
April, 2010	Annual Meeting
20 <sup>th</sup> May, 2010	Training event
13 <sup>th</sup> July, 2010	Training event
21 <sup>st</sup> July, 2010	Management Committee Meeting

### Meetings and events of the four BMS Research Infrastructures of the second generation

EMBRC	
Date	Title
18 <sup>th</sup> – 19 <sup>th</sup> June, 2009	Kick-Off meeting with all partners, new partners recruited, SZN Naples
17 <sup>th</sup> – 19 <sup>th</sup> September, 2009	WPs established, tasks distributed, provisional budget established, UPMC Paris
30 <sup>th</sup> October, 2009	Steering Group meeting, WP and provisional budget adjusted, SZN Naples
12 <sup>th</sup> – 15 <sup>th</sup> November, 2009	Partner meeting, budget finalised, CNRS Paris
26 <sup>th</sup> – 27 November, 2009	Partner meeting, proposal finalised, CNRS Paris
13 <sup>th</sup> – 14 <sup>th</sup> October, 2010	Meeting with Steering Committee, Partners and WP leaders, status report, OOV Villefranche

ERINHA	
Date	Title
09 <sup>th</sup> June, 2009	Project partner and Stakeholder meeting
21 <sup>st</sup> September, 2009	Project partner meeting
November, 2010	Kick-Off meeting

EU-OPENSREEN	
Date	Title
19 <sup>th</sup> May, 2010	Project partner meeting, Prague
22 <sup>nd</sup> – 23 <sup>rd</sup> November, 2010	Kick-Off meeting, Brussels

Euro-Biolmaging	
Date	Title
21 <sup>st</sup> – 22 <sup>nd</sup> September, 2009	1 <sup>st</sup> Stakeholder Meeting, Heidelberg
21 <sup>st</sup> – 22 <sup>nd</sup> October, 2010	2 <sup>nd</sup> Stakeholder Meeting, Vienna

## APPENDIX D LIST OF PROPOSALS ALREADY ON THE ESFRI ROADMAP IN PP

No.	Title	Acronym	Coordinator	Duration of the PP in months
<b>The six BMS Research Infrastructures of the first generation</b>				
1	Biobanking and Biomolecular Resources Research Infrastructure	BBMRI	Prof. Kurt Zatloukal (Austria) <a href="mailto:Kurt.zatloukal@meduni-graz.at">Kurt.zatloukal@meduni-graz.at</a>	36
2	European Advanced Translational Research Infrastructure in Medicine	EATRIS	Prof. Rudi Balling (Germany) <a href="mailto:Rudi.Balling@uni.lu">Rudi.Balling@uni.lu</a>	36
3	European Clinical Research Infrastructures Network	ECRIN	Prof. Jacques Demotes-Mainard (France) <a href="mailto:jacques.demotes@inserm.fr">jacques.demotes@inserm.fr</a>	36
4	European Life-science Infrastructure for Biological Information	ELIXIR	Prof. Janet Thornton (United Kingdom) <a href="mailto:thornton@ebi.ac.uk">thornton@ebi.ac.uk</a>	38
5	European Infrastructure for phenotyping and archiving of model mammalian genomes	INFRAFRONTIER	Prof. Martin Hrabé de Angelis (Germany) <a href="mailto:hrabe@helmholtz-muenchen.de">hrabe@helmholtz-muenchen.de</a>	36
6	Integrated Structural Biology Infrastructure	INSTRUCT	Prof. David I Stuart (United Kingdom) <a href="mailto:instruct@strubi.ox.ac.uk">instruct@strubi.ox.ac.uk</a>	36

No.	Title	Acronym	Coordinator	Duration of the PP in months
<b>The four BMS Research Infrastructures of the second generation</b>				
7	European Marine Biological Resource Centre	EMBRC	Prof. Roberto di Lauro (Italy) <a href="mailto:dilauro@szn.it">dilauro@szn.it</a>	36-48
8	European Research Infrastructure on Highly Pathogenic Agents	ERINHA	Dr. Hervé Raoul (France) <a href="mailto:herve.raoul@inserm.fr">herve.raoul@inserm.fr</a>	36
9	European Infrastructure of Open Screening Platforms for Chemical Biology	EU-OPENSREEN	Dr. Ronald Frank (Germany) <a href="mailto:info@eu-openscreen.eu">info@eu-openscreen.eu</a>	36
10	Research Infrastructure for Imaging Technologies in Biological and Biomedical Sciences	Euro-Biolmaging	Dr. Jan Ellenberg (Germany) <a href="mailto:jan.ellenberg@embl.de">jan.ellenberg@embl.de</a>  and Prof. Stefan Schönberg (Austria) <a href="mailto:stefan.schoenberg@medtech.uni-heidelberg.de">stefan.schoenberg@medtech.uni-heidelberg.de</a>	36-48



## APPENDIX E LIST OF PROPOSALS RECEIVED AND ASSESSED

### List of proposals provided to BMS TWG for assessment

No.	Title	Acronym	Scientific Area/ Expert Group	Submitted by
RU09_01	Infrastructure for Systems Biology-Europe	ISBE	Systems Biology	United Kingdom
RU09_09	Infrastructure for Analysis and Experimentation on Ecosystems	ANAEE	Green Biotechnology & Biological Sciences	France
RU09_10	Microbial Resource Research Infrastructure	MIRRI	Biorepositories - Microorganisms	France
RU09_17	European Animal BioBanking Infrastructure	EABB	Biorepositories - Microorganisms	Italy
RU09_18*	European infrastructure for QUALity of chemical and biological Measurements	Euro-QUAM		Italy
RU09_19*	Pollution effects on the sustainable use of Poplar as renewable resource	BIO3MASS		Italy
RU09_20	European Mediterranean Crop Systems Biology Institute	EMCSBI	Systems Biology	Italy
RU09_21	Bioscience center for bridging laboratory with agro-ecosystem analysis for climate change adaptation research	BRIDGE	Green Biotechnology & Biological Sciences	Italy
RU09_22	Mediterranean Biological Resources Center	MED.BANK	Green Biotechnology & Biological Sciences	Italy

\* not assessed by BMS TWG because out of the BMS TWG's scope

## APPENDIX F MEMBERS OF THE BMS EXPERT GROUPS

Batoko, Henri	University of Louvain, Belgium
Dudits, Dénes	Hungarian Academy of Sciences, Hungary
Falaschi, Arturo	International Centre for Genetic Engineering and Biotechnology (ICGEB), Italy
Heinegård, Dick	University of Lund, Sweden
Herault, Yann	Institute of Genetics and Molecular and Cellular Biology (IGBMC), France
Lawlor, David	Rothamsted Research, United Kingdom
Metspalu, Andres	University of Tartu, Estonia
Omholt, Stig	Norwegian University of Life Sciences, Norway
Pihlajaniemi, Taina	University of Oulu, Finland
Salkinoja-Salonen, Mirja	University of Helsinki, Finland
Serrão, Ester	University of Algarve, Portugal
Spiertz, Huub	University of Wageningen, The Netherlands
Thaller-Honold, Svetlana	VDI Technology Centre GmbH, Germany
Thanos, Dimitrios	Academy of Athens, Greece

## APPENDIX G LITERATURE

<sup>1, 4</sup> European Commission, Directorate Research, 2010 Report of the Expert Group on Research Infrastructures established by the European Commission to create “A vision for strengthening world class Research Infrastructures in the ERA”

<sup>2</sup> Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the regions towards Joint Programming in Research: Working together to tackle common challenges more effectively; Brussels, 15.7.2008 COM, (2008), 468 final

<sup>3</sup> European Council Conclusion of 16<sup>th</sup> June, 2010

<sup>5</sup> [www.esf.org/marineboard/publications/](http://www.esf.org/marineboard/publications/); “Marine Board Position Paper 15 on Marine Biotechnology”

<sup>6</sup> Meeting Europe’s Challenges: The Role and Importance of Biological and Medical Sciences Research Infrastructures, 2010

<sup>7</sup> see [ftp://ftp.cordis.europa.eu/pub/fp7/docs/report-meeting-eu-funded-biobanks\\_en.pdf](http://ftp.cordis.europa.eu/pub/fp7/docs/report-meeting-eu-funded-biobanks_en.pdf)

<sup>8</sup> Survey on Research Infrastructures in the area of agri-food research; Report from the Collaborative Working Group “Shared Infrastructures for European agri-food research” (SCAR CWG) to the Standing Committee on Agricultural Research (SCAR)

<sup>9</sup> ERA-Instruments – an ERA-Net initiative for promoting infrastructure funding in the Life Sciences; Dr. Johannes Janssen; Deutsche Forschungsgemeinschaft (DFG); Coordinator of ERA-Instruments; [www.era-instruments.eu](http://www.era-instruments.eu)

<sup>10</sup> ESF’s /EMRC’s Strategy for medical Research Infrastructures in Europe; Prof. Liselotte Højgaard, MD DMSc; Chair of the Standing Committee of the European Medical Research Councils (EMRC), European Science Foundation (ESF)

<sup>11</sup> Jean-Emmanuel Faure; European Commission, DG Research European Commission

<sup>12</sup> Remote Evaluation Process; Update of the Roadmap Research Infrastructures Thematical Working Group Biological and Medical Sciences; Procedural Guidelines for BMS Expert Groups



Biological and Medical Sciences  
Thematic Working Group  
Report 2010

Contact:  
ESFRI Secretariat  
Postal address:  
European Commission  
SDME 01/128  
B-1049 Brussels, Belgium  
Tel: +00 32 2 299 25 39  
Fax: +00 32 2 299 21 02  
ESFRI@ec.europa.eu  
[www.ec.europa.eu/research/esfri](http://www.ec.europa.eu/research/esfri)



European Strategy Forum  
on Research Infrastructures