

# The European Research Infrastructures of the ESFRI Roadmap in Biological and Medical Sciences: status and perspectives

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## Abstract

**Introduction.** Since 2002, the European Strategy Forum on Research Infrastructures identified the needs for Research Infrastructures (RIs) in Europe in priority fields of scientific research and drafted a strategic document, the ESFRI Roadmap, defining the specific RIs essential to foster European research and economy. The Biological and Medical Sciences RIs (BMS RIs) were developed thanks to the active participation of many institutions in different European member states associated to address the emerging needs in biomedicine and, among these, the Italian National Institute of Health (ISS), in virtue of its role in public health and research, has been specifically involved in the national development and implementation of three RIs: the Biobanking and Biomolecular Resources Research Infrastructure (BBMRI), the European Advanced Translational Research Infrastructure in Medicine (EATRIS) and the European Clinical Research Infrastructures Network (ECRIN).

**Aim.** This article outlines the design and development of these RIs up to the recent achievement of the ERIC status, their importance in the Horizon 2020 programme and their societal and economic potential impact, with special attention to their development and significance in Italy.

**Conclusions.** The ISS plays a unique role in fostering a coordinated participation of excellence Italian institutes/facilities to different European biomedical RIs, thus contributing to health innovation, healthcare optimization, and healthcare cost containment.

## Key words

- ESFRI
- translational medicine
- healthcare economics
- research infrastructures

## INTRODUCTION

Research Infrastructures (RIs) are facilities, resources or services that constitute large sets of research equipment or instruments and represent or complement knowledge resources such as collections, archives and databases. RIs can be concentrated on a single spot, distributed or virtual (enabling services electronically). They often require a structured information system for data management and for enabling information and communication [1].

To avoid duplication of similar RIs in the European area and to foster a coordinated approach regarding public policies and funding, at the beginning of 2002, the European Strategy Forum on Research Infrastructures (ESFRI) was established on proposal by the Council of the European Union. Constituted by delegates of Research Ministries of the Member States and Associated Countries and including a representative of European Commission (EC), the ESFRI has the objective of identifying and addressing the scientific needs

of RIs in Europe for the next 10-20 years. Its mission is to support a coherent and strategy-led approach to policy-making on new and existing pan-European and global RIs. The ESFRI Roadmap was first published in 2006, where 35 projects were identified in all the fields of science [2]. The Roadmap was updated by ESFRI in 2008 and 2010, bringing the total number of RIs of pan-European relevance to 48 [1, 3]. The ESFRI Roadmap addresses all scientific disciplines that require a large scale RI with a joint effort on European or international scale. The proposed infrastructures are grouped by research field: Social Sciences & Humanities, Environmental Sciences, Energy, Biological and Medical Sciences, Material Sciences and Analytical Facilities, Physical Sciences & Engineering. These projects are very diverse in size and character and are at very different stage of development.

The implementation of the projects on the ESFRI Roadmap is a priority for both ESFRI and the EC; for this reason, the ESFRI Implementation Group was set

up in 2011 to address issues related to the acceleration and improvement of the implementation and procedures of RIs. According to Implementation Group (IG) definitions [4], an ESFRI project can be considered to be under implementation when the following conditions are met: i) agreed statutes or other legal provisions for the construction and operation of the RI are present; ii) a stable legal governance structure is in place; and iii) there is budget commitment for the different stages of the RI. Moreover, the IG considers an ESFRI project to be in the preparatory phase, when it has an officially allocated budget from the European Commission for a specific time period in order to arrange the legal, governance and financial conditions to start the implementation of the project. The IG also defines the interim phase for projects that ended the official preparatory phase, but that do not yet meet the legal, governance and financial conditions that are necessary to be considered as under implementation.

According to the EC Memo [5] on ESFRI RIs published in 2012, about half of the ESFRI projects are now in their implementation phase. These RIs are listed in *Table 1*.

### FROM RI PROJECTS TO EUROPEAN RESEARCH INFRASTRUCTURE CONSORTIUM (ERIC)

A major difficulty in setting up pan European RIs was the lack of an adequate legal framework allowing the creation of appropriate partnerships. In an attempt to enhance flexibility and opportunities for RIs, the European Council, responding to requests from EU countries and the scientific community, introduced a scheme for better governance through a new legal framework, the European Research Infrastructure Consortium (ERIC) [6]. ERIC aims to facilitate the joint establishment and operation of RIs involving at least three Member States on the basis of Article 171 of the European Treaty [7]. RIs in the ERIC framework will be able to operate as legal entities, adapting their individual specific requirements and enhancing their flexibility and capability in attracting funding from various sources (non-EU countries, private sector).

On 3 December 2012, the Commission adopted a proposal for a Council Regulation amending the Regulation EC 723-2009 concerning the ERIC [8]. The aim was to facilitate the participation of associated countries in ERICs and ensure that their contributions to ERICs are reflected in terms of voting rights on the same footing as Member States for ERICs that are hosted by the associated countries.

To set up an ERIC, the following steps are necessary:

- at least three Member States must agree to establish and operate together a research infrastructure. Associated countries, third countries and intergovernmental organizations may also be members;
- the members agree on statutes ruling governance, intellectual property rights policy, financing, etc.;
- the seat has to be in an EU-Member State or in a country associated to the EU Framework programs;
- the members submit the file to the Commission, which, with the aid of independent experts, examines

whether the conditions of the ERIC Regulation are fulfilled. After that, a committee composed of representatives of the EU Member States gives an opinion on the file by qualified majority, following which the Commission decides on the application.

The application is valid if it is supported by at least three Member States and shall contain: i) the proposed statutes of the ERIC; ii) the technical and scientific description of the infrastructure (business plan); iii) the declaration of the host Member State recognizing the ERIC as an international organization exempted from VAT and excise duty according to the pertinent directives; iv) the agreement between the Members of the ERIC on the limits and conditions of the tax exemption.

To date, six RIs (CLARIN, SHARE, EATRIS, ESS, ECRIN and BBMRI) (*Table 1*) have been established as ERIC ([http://ec.europa.eu/research/infrastructures/index\\_en.cfm?pg=eric](http://ec.europa.eu/research/infrastructures/index_en.cfm?pg=eric)). Five other applications have been received at the Commission at the present time (*Table 1*).

### BIOLOGICAL AND MEDICAL SCIENCES RIs (BMS RIs) AND THE ITALIAN ROADMAP

The pan-European BMS RI projects on the ESFRI roadmap provide an interdisciplinary, innovative environment in the field of life sciences and health research where world-leading investigators conduct forefront research using open access to cutting-edge technologies and scientific data. BMS RIs will play a key role in closely linking basic research to medical application, providing services, training and access to technology for scientists in academia as well as industry.

Among the BMS RIs, on November 2013 the Biobanking and Biomolecular Resources Research Infrastructure (BBMRI), the European Advanced Translational Research Infrastructure in Medicine (EATRIS) and the European Clinical Research Infrastructures Network (ECRIN) were awarded the ERIC status by the EC.

#### BBMRI

Early in 2009 *TIME Magazine* identified biobanks as one of the 10 ideas changing the world [9] and ESFRI recognized in the first roadmap the research biobanking as an area of strategic European interest [10]. Consistent with this vision, a pan-European BBMRI for biomedical and biological research in Europe was funded ([www.bbMRI.eu](http://www.bbMRI.eu)). The project intended to meet the growing need for harmonized approaches to establish and manage biorepositories, and for the implementation of a European infrastructure built on existing sample collections, resources, technologies and expertise, connecting them in a European network.

The mission of BBMRI is to sustainably secure access to biological resources required for health-related research intended to improve the prevention, diagnosis and treatment of disease as well as to promote the health of the European citizens. Biomedical quality-assessed samples and data are essential for academic and industry-driven research to treat and prevent human diseases [11, 12].

BBMRI has the following objectives:

- harmonizing standards for sample collection, storage and analysis;

**Table 1**  
Research infrastructures in the implementation phase [5]

Category	RI short name	Name	Mission
Social Sciences and Humanities	CESSDA	Council of European Social Science Data Archives	To provide and facilitate access for researchers to high quality data for social sciences
	CLARIN-ERIC*	Common Language Resources and Technology Infrastructure	To advance research in humanities and social sciences by giving researchers unified single sign-on access to a platform which integrates language-based resources and advanced tools at a European level
	DARIAH**	Digital Research Infrastructure for the Arts and Humanities	To enhance and support digitally-enabled research across the humanities and arts
	ESS-ERIC*	European Social Survey	To chart and explain the interaction between Europe's changing institutions and the attitudes, beliefs and behavior patterns of its diverse populations
	SHARE-ERIC*	Survey of Health, Ageing and Retirement in Europe	To build an infrastructure of micro data of households and individuals necessary to understand individual and societal ageing
Environmental Sciences	ICOS**	Integrated Carbon Observation System	To provide the long-term observations required to understand the present state and predict future behavior of the global carbon cycle and greenhouse gas emissions
	EURO-ARGO**	Global Ocean Observing Infrastructure	To allow active coordination and strengthening of the European contribution to the international Argo programme, source of information and data over the ocean's interior
	Lifewatch**	Science and Technology Infrastructure for Research on Biodiversity and Ecosystems	To provide an analytical platform for the modelling and simulation of both existing and new data on biodiversity to enhance the knowledge of biodiversity functioning and management
Energy	JHR	Jules Horowitz Reactor	To study the materials and fuel behavior for nuclear power plants
Biological and Medical Sciences	BBMRI-ERIC*	Biobanking and Biomolecular Resources Research Infrastructure	To form an interface between biological specimens and data (from patients and European populations) and top-level biological and medical research
	EATRIS-ERIC*	European Advanced Translational Research Infrastructure in Medicine	To provide a new development pathway, open to researchers and companies in need of support for advancing biomedical innovations
	ECRIN-ERIC*	European Clinical Research Infrastructures Network	To support multinational clinical research projects in Europe
	ELIXIR	European Life-science Infrastructure for Biological Information	To act as a platform for collection, storage, validation, dissemination and utilisation of biological data
	INFRAFRONTIER	European Infrastructure for Phenotyping and Archiving of Model Mammalian Genomes	To provide access to scientific platforms, data and services for the systemic phenotyping, archiving and distribution of mouse models
	INSTRUCT	Integrated Structural Biology Infrastructure	To provide open access to state-of-the art structural biology technologies for researchers

(continues)

Table 1 (Continued)

Materials Sciences	<b>ESFR</b>	European Synchrotron Radiation Facility	To operate the most powerful high energy synchrotron light source in Europe and bring together a wide range of disciplines including physics, chemistry and materials sciences as well as biology, medicine, geophysics and archaeology
	<b>ESS*</b>	European Spallation Source	To complete and operate the best and most powerful neutron source in the world by the end of the decade
	<b>ILL 20/20</b>		To act as a productive and reliable source of slow neutrons for the study of condensed matter
	<b>European XFEL</b>	European Hard X-ray Free Electron Laser	To be a world leading facility for the production of intense, short pulses of X-rays for scientific research in a wide range of disciplines
	<b>E-ELT</b>	European Extremely Large Telescope	To be the largest optical/near-infrared telescope in the world
	<b>SKA</b>	Square Kilometre Array	To be the world's largest and most sensitive radio telescope
	<b>ELI</b>	Extreme-Light-Infrastructure	To provide high-quality access to the international research community for prospective applications of ultra-intense and ultra-short laser pulses
	<b>FAIR</b>	Facility for Antiproton and Ion Research	To provide high energy primary and secondary beams of ions of highest intensity and quality, including an 'antimatter beam' of antiprotons allowing forefront research in different disciplines of physics
	<b>SPIRAL 2</b>	Facility for the production and study of rare isotope radioactive beams	To deliver stable and rare isotope beams with intensities not yet available with present machines
<b>E-infrastructure</b>	<b>PRACE</b>	Partnership for Advanced Computing in Europe	To provide access to distributed pan-European world class high performance computing and data management resources and services

\*RIs which have been established as ERIC

\*\*Facilities which have submitted ERIC application to EC

- harmonizing data collection and the associated database infrastructure;

- providing ethical and legal guidance;

- developing a sustainable funding model for biobanks.

During the preparatory phase, ended in January 2011, BBMRI has grown into a 54-member consortium with more than 225 associated organisations, largely biobanks from over 30 countries, establishing an interactive catalogue of associated biobanks ([www.bbmri.eu](http://www.bbmri.eu)). At the end of the preparatory phase, 14 Member States signed the declaration of intention (Memorandum of Understanding) to participate in BBMRI-ERIC. During this phase, BBMRI Charter, Statute and business plan, necessary to activate the formal request of the consortium to the EC, have been refined and adopted.

On August 9<sup>th</sup>, 2012 BBMRI-ERIC application has been submitted to EC. Hence BBMRI is now approaching the operative phase with a headquarter in Graz (Austria) and common services in other Member countries. In each participating State, according to BBMRI Statutes, a National hub to coordinate the activities of the national biobanks and to interface the European central coordination headquarter has been established. The BBMRI-ERIC Inauguration Conference took place on September 16<sup>th</sup>, 2013 and during the event National Nodes have been formally presented and on November 22<sup>nd</sup> 2013, BBMRI was of-

ficially awarded the Community legal framework for a ERIC ([http://ec.europa.eu/research/infrastructures/index\\_en.cfm?pg=eric](http://ec.europa.eu/research/infrastructures/index_en.cfm?pg=eric)). In continuity with the work performed during the preparatory phase, the Istituto Superiore di Sanità (ISS), by a joint mandate of the Italian Ministries of Health and Education, University and Research, signed the national participation to BBMRI-ERIC and established the National Node of BBMRI ([www.bbmri.it](http://www.bbmri.it)). The Italian node of BBMRI has held its launch or "kick-off" meeting on October 8<sup>th</sup>, 2013 during the ESBB's Annual Conference ([www.esbb.org/verona/](http://www.esbb.org/verona/)).

So far the founding BBMRI-ERIC members are: Austria, Belgium, Czech Republic, Estonia, Finland, Greece, Italy, the Netherlands, Malta, Sweden, France, Germany, Norway, Poland, Switzerland and Turkey joined as Observer member.

### EATRIS

In recent years, a large number of editorial articles published in top journals have emphasized the importance of strategic national and international initiatives for the promotion of biomedical translational research [13]. In fact, there is a general concern (shared by the scientific community, patients' organizations, policy-makers and national governments) about major bottlenecks which hamper the translation of the results stemming from basic research into clinical experimen-

tation and medical practice. In 2006 a European call for proposals for preparatory phase for the construction of some European RIs particularly relevant for the promotion of biomedical translational research of advanced therapies was launched. Among the proposals, the EATRIS turned out to be one of special potential importance for the development of biomedical translational research and advanced therapies. In fact, an evaluation process assessing scientific excellence, impact, and possible implementation identified EATRIS proposal as one of the six projects to receive 7<sup>th</sup> Framework Program (FP7) funding for a preparatory phase (2008-2010).

After this preparatory phase and a one-year transition phase supported by the participating Member States, in 2012 EATRIS entered its construction phase (Partners carry out construction on major upgrade as agreed in consortium agreement). In 2011 the EATRIS headquarters (namely EATRIS Coordination and Support) were opened in Amsterdam. These headquarters function as a broker office matching clients and translational service providers. On the 1<sup>st</sup> of June 2012, EATRIS applied for the legal status of ERIC with the support of 9 Member States (Czech Republic, Denmark, Spain, Finland, France, Italy, Norway, Estonia, The Netherlands).

From the 7<sup>th</sup> of November 2013 EATRIS is a new official European organisation under the ERIC framework ([http://ec.europa.eu/research/infrastructures/index\\_en.cfm?pg=eric](http://ec.europa.eu/research/infrastructures/index_en.cfm?pg=eric)).

EATRIS aims to support academia, SME's and large industry in translating results from bench to bedside by providing high quality services necessary for European researchers interested in the transfer of their discoveries into clinical studies (up to the early Phase II trials).

The translational research areas of focus for EATRIS Centres are based on product types as well as disease areas. The 5 product types covered in EATRIS (molecular imaging and tracing, vaccines, biomarkers, small molecules and advanced therapeutic medicinal products) cover the range of applications from preventive agents via diagnostics to therapeutics and they also reflect the areas of greatest potential in translational research and collectively offer a vastly superior research structure with respect to that possible with individual institutions.

Each country is represented by one or more research institutions or national networks, which constitute a national node ([www.eatris.eu](http://www.eatris.eu)). The ISS was delegated by the Italian Ministry of Health, in agreement with the Italian Ministry of Education, University and Research, to participate in the EATRIS preparation and transition phases and, more recently, to represent Italy in signing the formal participation to the EATRIS-ERIC. The ISS also promoted the participation of several other Italian institutions and networks in EATRIS creating the initial national node of EATRIS, named IATRIS (Italian Advanced Translational Research Infrastructures in Medicine) ([www.iatris.it](http://www.iatris.it)). IATRIS' main objective is to overcome the bottlenecks which delay both the transfer of basic research results into clinical applications and the feedback of clinical observations to the basic investigation. IATRIS represents a unique network of

academic institutions and research entities finalized to provide open multidisciplinary services and centralized facilities instrumental for projects of translational medicine under a national coordination. Most detailed information concerning the participating institutions and ongoing initiatives can be found on the IATRIS website ([www.iatris.it](http://www.iatris.it)). All this is expected to ensure a more effective and rapid transfer of the scientific knowledge into prevention, diagnosis and treatment of diseases. IATRIS will represent the Italian infrastructure system in EATRIS-ERIC.

### ECRIN

ECRIN is a distributed ESFRI roadmap RI designed to promote cooperation in clinical research in Europe. ECRIN was listed on the first edition of the ESFRI Roadmap and it began as a European research project funded under the Framework Programme 6 (FP6).

The current RI is the result of several EU projects carried out in recent years: i) the FP6 ECRIN-RKP project (Reciprocal Knowledge Programme, 2004-2005) helping to identify the bottlenecks and define a strategy; ii) the FP6 ECRIN-TWG (Transnational Working Groups, 2006-2008) leading to the development of generic tools and procedures for multinational clinical research; and iii) the FP7-funded preparatory phase (ECRIN-PPI, Preparatory Phase for the Infrastructure, 2008-2011), designed to further structure the RI and to start provision of support to 'pilot' multinational clinical studies, in order to test the organization and the procedures.

The new FP7-funded project ECRIN-IA (ECRIN Integrating Activity, 2011-2015) aims to help ECRIN expand the infrastructure created through the previous phases and plans, among other objectives, to support the structuring of networks in three strategic areas (rare disease, medical devices and nutrition) [14].

The mission of ECRIN is to:

- facilitate the conduct of multinational clinical studies in Europe by harmonizing national procedures and providing a "one-stop-shop" network of services to investigators and sponsors in multinational clinical research studies, mainly in the academic and SME sector;
- improve the quality and efficiency of European clinical research, ensuring scientific excellence to clinical research projects [15];
- lay the foundations for a more effective international cooperation, able to boost European research, in order to make Europe a single area for clinical research.

ECRIN is based on the connection of national networks of academic infrastructures for clinical research, Clinical Research Centres and Clinical Trial Units, able to provide information, consultancy and services for multinational clinical trials ([www.ecrin.org](http://www.ecrin.org)).

Currently it covers 14 European countries (Austria, Belgium, Denmark, Finland, France, Germany, Hungary, Ireland, Italy, Poland, Spain, Sweden, Switzerland and the UK) mainly participating with national nodes/hubs or with institutions directly or indirectly involved in clinical research. All institutions or national nodes/hubs are connected to the central coordination body, established in Paris at INSERM, through the network of European Correspondents (EuCos).

ECRIN has recently acquired the ERIC status ([http://ec.europa.eu/research/infrastructures/index\\_en.cfm?pg=eric](http://ec.europa.eu/research/infrastructures/index_en.cfm?pg=eric)): Italy signed the statutes as a Member together with Germany, Spain, Portugal and France (host country and coordinator of the consortium). The ERIC status will allow ECRIN to act as a single international legal entity and will provide with the capacity to propose a single task delegation contract with the sponsor of the clinical trial [14].

### RIS IN THE COMING 8<sup>TH</sup> FRAMEWORK PROGRAMME FOR RESEARCH AND INNOVATION “HORIZON 2020”

“Horizon 2020” is the new, integrated funding system that will cover all research and innovation funding currently provided through the Framework Programme for Research and Technical Development, the Competitiveness and Innovation Framework Programme (CIP) and the European Institute of Innovation and Technology (EIT), bringing together these different types of funding in a coherent and flexible manner. This € 80 billion package for research and innovation funding will enter into force on 1<sup>st</sup> of January 2014, after the end of FP7 on 31<sup>st</sup> of December 2013, and will run from 2014 to 2020, with the aim to secure global competitiveness and create new growth and jobs in Europe. Horizon 2020 will be based on three main themes: excellence in science, tackling societal challenges and creating industrial leadership and competitive frameworks.

In the European scenario, RIs are seen as pivotal instruments to foster innovation through international cooperation, provided these instruments are used wisely and efficiently. Indeed, in order to help Europe to respond to grand challenges in science, industry and society, there is a need to ensure the implementation, long-term sustainability and efficient operation of new and existing RIs. For this reason, RIs have been recognized as one of four key objectives of the “Excellent Science” pillar within the EC’s proposal for Horizon 2020 [16]. In particular, funding of European RIs will contribute to:

- facilitate and support the implementation and operation of ESFRI and other world-class research infrastructures;
- integrate and facilitate access to national research infrastructures;
- continue supporting the development, deployment and operation of e-infrastructure;
- foster the innovation potential of research infrastructures and their human capital;
- reinforce the European policy and international co-operation.

### RIs IN THE INNOVATIVE MEDICINES INITIATIVE 2 (IMI 2) RESEARCH FUNDING INITIATIVE

IMI 2 ([www.imi.europa.eu/content/imi-2](http://www.imi.europa.eu/content/imi-2)) is a Joint Technology Initiative (JTI) bringing together companies, universities, public laboratories, innovative SMEs, patient groups and regulators. It will pave the way for breakthrough vaccines, medicines and treatments to tackle Europe’s growing health challenges through a

concentrated and combined science and innovation effort. It will help secure the future international competitiveness of Europe’s pharmaceutical industry.

The aim of IMI 2 is to enable an appropriate European-level research and innovation response that will make a crucial contribution to delivering better health and wellbeing for all, and positioning Europe as a leader in the rapidly expanding global markets for health and wellbeing innovations.

Delivering innovative solutions can only be achieved through combining the expertise of large and mid-size pharmaceutical and biotech companies (and associated contract research organizations), academia, patients’ organizations, regulatory bodies, health technology agencies (HTA) and health authorities, all having a shared desire to change and improve the current health-care ecosystem.

Specifically IMI 2 will:

- create cross disciplinary research to improve the efficiency of the entire medicines development process from discovery all the way through to patient access, thus improving access, quality and cost for more sustainable health systems;
- conduct collaborative research focusing directly on generating innovative preventive and therapeutic treatment options addressing priority healthcare challenges for Europe (*i.e.* where the burden of disease is the highest, not just of primary care but on the entire social security and labour system);
- provide a transparent platform facilitating engagement of all key stakeholders in the provision of healthcare (*i.e.* healthcare practitioners, regulators, HTA agencies, patients and payers) to ensure that new scientific advances are translated into effective healthcare solutions;
- provide training and infrastructure needs to support effective implementation of the research outcomes;
- drive widespread translation of the resulting and existing knowledge into innovative, effective products, strategies, interventions and services through long term and coordinated co-operation between all players in the healthcare ecosystem;
- create an integrated R&D framework that will attract investment and in turn strengthen the competitiveness of the European-based industries, creating new market opportunities increasing employment and economic growth.

The new scenario of the establishment of three main RIs strategically important for biomedical research (EA-TRIS, ECRIN and BBMRI) and the concomitant progress in the development of all other relevant RIs in the field of biomedical sciences – ERINHA for high safety level laboratory, Euro-bioimaging for biomedical imaging infrastructure, Openscreen for screening platforms for chemical biology, and ELIXIR which underpins biological information and data storage for biomedical research – will facilitate the cooperation between all these RI frameworks and the newly proposed public-private partnership (IMI 2), strengthening Europe’s impact in the area of biomedical research, further enhancing attractiveness for global cooperation and collaboration, and ensuring efficient use of available research funding.

The new IMI 2 JTI is expected to start in January 2014 and end in 2024. It will bring together the members of the European Federation of Pharmaceutical Industries and Associations (EFPIA) and will also be open to other industries and sectors.

IMI 2 is based on equal sharing of cost between the EU budget and the private sector. The estimated budget of IMI2 is € 3.45 billion. The EU will contribute up to € 1.725 billion from Horizon 2020, the next EU research and innovation programme. This will match the in-kind EFPIA commitment of up to € 1.5 billion and an additional amount of up to € 225 million if other life science industries will decide to join and contribute to IMI 2 as members or associated partners in individual projects.

### THE ECONOMIC AND SOCIETAL IMPACT OF RIs

RIs are instrumental for the advancement of science and stimulate, through their excellence in research, innovation, learning and education processes, that are highly important for society and economy. In particular, the creation of the BMS RIs throughout Europe is expected to strengthen the scientific competitiveness of Europe as well as the attractiveness for industry, by producing high quality tools and instruments and providing access to resources developed by all the European countries (healthcare databases, genetic databases, etc.) [11-14]. Furthermore, large RIs are strategic instruments to increase scientific integration within European countries and to reduce inequalities between them, fostering cooperation and providing the research community with the required access to innovative methods and technologies. By favoring a climate of collaboration, sharing and exchange of knowledge, RIs can further strengthen the European position by encouraging mobility, improving training and education, and attracting the best researchers from around the world. Thus, RIs can significantly contribute to human capital development, which is highly relevant for the local, national and European economy and for the society in general.

Concerning the benefits for researchers, the access to European facilities could trigger a positive mechanism on research. In fact, the use of a European infrastructure by international researchers is based on a peer-reviewed system, which impels the facility's management to continuously evaluate and improve the standard of the equipment and the quality of the service. This also incentivizes the "local" user community to improve the quality of their access research proposals inducing a wider improvement in the quality of research and a greater effort to exploit and publish the outcomes of their use [17].

The participation in European RIs will also create the opportunity for access to European funding within Horizon 2020 framework, and will have an indirect impact at the national level by acting as an incentive to invest in national infrastructures and to promote translational and clinical research. The Italian participation in European RIs is expected to exert a positive impact on the Italian health system, in view of the RI importance in

fostering translational medicine and of the future challenges for combining needs in public health and economic availability.

### CONCLUSIONS

Consistently with its mission of promoting translational research finalized to public health, the ISS has played a crucial role in ensuring and coordinating the Italian participation to three main BMS RIs (BBMRI, ECRIN and EATRIS), which have recently received the formal recognition of the ERIC status by the European Commission (EC).

This role has important implications both at a national level, where is mandatory to ensure a coordinated and qualified participation of many different institutions to these RIs, and at a European level. Notably, a national coordination for interconnected RIs is consistent with the EC policy, that oversees for the next future a strong interoperability among different RIs and continent-wide initiatives to face public health challenges.

From the national point of view, health services are decentralized in Italy from central to regional level of government and all stakeholders (national and regional) have their important relative weight. Thus, there is the urgency of finding well-established innovative solutions to rationalize integration of health knowledge into innovation, cost-saving and health improvement.

In conclusion, interposed between regions and Europe, the ISS, as the major national research institute on public health in Italy, can play a unique role in allowing a coordinated participation of excellence centers and reference institutes/facilities located in different regions to these European RIs and is called to the urgent challenges of integrating and synergizing the investment in high-quality RIs, with the objective to allow major return through value generated by health innovation, healthcare optimization, and healthcare cost containment [11-14].

### Author's contribution statement

FP, EB e FB planned the article, sections articulation and revised the final version. AC, AV and FC drafted the first version of most of the sections, while MN and MV contributed to complete the article. All the authors discussed and approved the final manuscript.

### Conflict of interest statement

All authors have no financial interest related to the material in the manuscript.

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