Medical Research Infrastructures: Solid foundations for Horizon Europe

BBMRI-ERIC, EATRIS-ERIC and ECRIN-ERIC are ESFRI medical research infrastructures (RI) with an ERIC status (European Research Infrastructure Consortia[1]), established as **high quality service providers** for academia and industry. Through our services, we support discovery, translational and clinical research, underpinning a common objective – **creating, developing and delivering new value to European patients.**

Building on each RI individual capabilities and networks, we are fully aware of the critical importance to accelerate and deepen collaboration among medical ERICs, to increase the chances of high quality European medical research to reach the patient with significant impact. With this objective in mind, we continue to develop interoperable tools, shared activities, joint services and common strategies on **quality, standards** and **advocacy** to maximise the societal impact of Europe's excellent research efforts.

We fully embrace the mission-oriented approach as suggested by Professor Mazzucato, to tackle the research and innovation challenges ahead, and as recently adopted in the Commission proposal for Horizon Europe. Such approach is complementary to the multi-disciplinary collaborative vision and transnational frameworks already implemented by the sustainable medical ERICs, and will be decisive in addressing the longstanding obstacles, particularly hampering health research in Europe. **Cross-sector collaboration is of the utmost importance to generate impact for patients**.

The **ESFRI roadmap** and the **development of the ERIC Forum**[2] have already created a robust framework for supporting the scientific and technological needs of the scientific community. The RIs provide a solid foundation for scientific development by creating a critical mass of complementary capacities to tackle the ambitious challenges identified as Missions. **In the field of medical research, a federated alliance of BBMRI, EATRIS and ECRIN guarantees the promotion of innovation and knowledge, and the involvement of all parties needed to push forward novel therapies in the European Research Area (ERA), and their optimal use in individual patients.**

For the upcoming framework programme to be as innovative and successful for health research in Europe as possible, **the medical ERICs consider four critical success factors for Horizon Europe**:

- *Avoid undesired duplication and fragmentation;*
- *Safeguard quality and enhance reproducibility;*
- *Support public engagement by promoting responsible research policies;*
- *Enable rigorous innovation management.*

1. Avoid undesired duplication and fragmentation

The ERA suffers from substantial duplication and fragmentation of strategies, expertise and services, due to the broad range of stakeholders required in the medicines development pipeline, which often results in competition rather than cooperation, and in the creation of silos. In addition, national regulation, organisation and funding of medical research is a major source of duplication and fragmentation. Such a fragmented environment creates an unbalance between the level of outcomes

[1] The community legal framework for a European Research Infrastructure Consortium (ERIC) is a specific legal form to facilitate the establishment and operation of research infrastructures with European interest. More information: https://ec.europa.eu/research/infrastructures/index.cfm?pg=eric

[2] https://www.eric-forum.eu/

(new treatments) versus investments. Horizon Europe has the opportunity to send a clear message to society that a knowledge-based ecosystem has the assets to tackle the major challenges of our time. Particularly in the field of health, the current health R&D socio-economic paradigm leaves many challenges unmet, such as the long-term sustainability of healthcare systems in an ageing population.

For the successful development of Horizon Europe, ***researchers should have effective access to existing high quality tools and coordinated services that have been developed by ERICs*** *to offer consistent and comprehensive support, as well as* ***promoting interdisciplinary and multinational research*** *aligned in the pursuit of excellence and impact.*

By providing scientists from any European country with efficient access to academic expertise and facilities, the medical ERICs are at the forefront of the battle against duplication and fragmentation; this has been recently addressed one step further by piloting a new joint service as part of the H2020-funded CORBEL project gathering 13 biological and medical RI[3]. Via a unique application, researchers could apply for the complementary expertise of the three medical ERICs for complex multimodal biomarker profiling[4]. Following this successful experience, additional joint services will be offered in the future to multinational projects, particularly in the field of precision medicine, which requires access to a seamless innovation pipeline from basic research to the patient.

2. Safeguard quality and enhance reproducibility

One of the fundamental principles of the scientific process is reproducibility – the idea that a discovery is valid only if another scientific team in a different laboratory can conduct the same experiment under the same conditions and obtain the same results. Recent studies[5] in the field of biomedical research show that findings from **an alarmingly high percentage of scientific papers cannot be reliably reproduced by other researchers.** The current situation results from a combination of the inherent complexity of scientific research, of technological and methodological innovation, of a lack of accountability for researchers, and of incentives created by a publish-or-perish culture in academia.

The tremendous effort in recent years to open up biomedical science, improve research efficiency and battle research waste through the European Open Science Cloud (EOSC) initiative and the FAIR principles is welcome and timely, with all three medical ERICs having endorsed the EOSC declaration.

However, most of the variability that causes biomedical research to be non-reproducible occurs in the laboratory before data is generated[6]. ** This questions the methodology, bias containment, statistical power, the need for multicentre experiments, and the quality management in research activities. Failing to act on these issues under Horizon Europe would have vast ramifications, including the continued lack of efficiency of biomedical research. **This is a particularly urgent matter as the healthcare systems

[3] http://www.corbel-project.eu/home.html
[4] http://www.corbel-project.eu/open-call/access-tracks/access-track-5-complex-multimodal-biomarker-profiling.html
[5] Florian Prinz, Thomas Schlange, and Khusru Asadullah (2011) Believe it or not: how much can we rely on published data on potential drug targets? Nature Reviews Drug Discovery, 10(9): 712. C
[6] Freedman LP, Cockburn IM, Simcoe TS (2015)The Economics of Reproducibility in Preclinical Research.PLoSBiol13(6):e1002165. doi:10.1371/journal.pbio.1002165

responsible for the implementation process of medical interventions cannot afford "failure," particularly in clinical practice.

*Horizon Europe should develop policies and instruments to ensure that the **methodology, quality and reproducibility of translational and clinical research are optimal, for more cost-effective research outcomes and a trustworthy scientific basis for clinical decision-making**. This can be achieved in part by **fostering the use of quality services and research laboratories** with sufficient quality measures and processes in place.*

A key mandate as medical ERICs is to provide access to research facilities of excellence, therefore to ensure that research quality is safeguarded through the **establishment of quality standards** and the dissemination (and adoption) of **best practices** by its members as well as the broader biomedical community. We have already implemented solutions to address this systemic issue of reproducibility: for instance, initiatives such as the BBMRI-ERIC quality management service[7] or the ECRIN data centre certification programme[8] can provide free, pre-competitive support to researchers to abide by ISO-CEN standards and international consensus guidelines. Additionally, EATRIS operates a bottom-up Quality Initiative encompassing multiple actions around reproducibility, standards, and reference materials[9]. Together with the EATRIS Inside programme that supports research funders and their investigators in designing high quality, robust translational research projects, the medical ERICs offer a wide range of support options related to quality.

3. Support public engagement by promoting responsible research policies

Public engagement in biomedical research is key for better health outcomes. Despite increased involvement of patient organisations and advocacy groups as partners in H2020 or IMI-funded research projects, **public and patient engagement is still often perceived as a "tick-box exercise" for researchers seeking funding**, especially when patients' participation comes too late in the proposal preparation process to make a difference.

*Horizon Europe should **enable a much needed cultural shift in the way academia, regulators, industry, and HTA bodies collaborate together with patient organisations**. The programme should be the vehicle for increased **multi-stakeholder and cross-sectoral collaboration**, providing **sustainable** and **meaningful opportunities for patients to participate** in the research process.*

Medical ERICs rely on the expertise of academic consortia. In order to carry out our missions effectively, our work depends strongly on facilitating the collaboration of multiple stakeholders (patients, citizens, industry, academia, healthcare professionals). BBMRI-ERIC involves patients and consumers in its decision-making process, via its ad-hoc advisory board called BBMRI Stakeholder Forums[10], to collate the input of the broad stakeholder community of the infrastructure, comprising patients, clinicians, funders, industry and other users. EATRIS has since 2015 its Patient Advisory Committee[11], aiming at bringing the patient's perspective in the evaluation process of research projects it supports. As part of the CORBEL

[7] http://www.bbmri-eric.eu/services/quality-management/
[8] http://www.ecrin.org/activities/data-centre-certification
[9] https://eatris.eu/insights/eatris-annual-report-2017/
[10] http://www.bbmri-eric.eu/BBMRI-ERIC/stakeholder-forum/
[11] https://eatris.eu/insights/egan-and-eatris-eric-sign-letter-of-intent/

project, ECRIN leads the Medical Infrastructures User Forums (MIUF)[12], a series of yearly meetings gathering RI representatives, funders and users to increase mutual awareness and generate collaboration opportunities.

4. Enable rigorous innovation management

The translation of scientific discoveries into tangible innovative interventions for patients is at the heart of medical ERICs' mission, and a top-priority societal challenge. However, despite a strong scientific case, **principal investigators often lack access to the methodology and services** needed for the seamless **development** of their potential future treatment or tool, therefore resulting in **increased research and funding waste**. Additionally, academia may lack knowledge and tools to develop successful industry partnering strategies or long-term public-private collaborations. A consequence, the **medical innovation continuum is extremely expensive** (drug development is estimated to be ca. USD2.5 billion per new marketed drug[13]) **time consuming** (the average period between discovery and development of. a new treatment is 10 years[14]) and comes with **enormous failure rates[15]**. For example, in clinical trials the probability of advancing from phase 2 to phase 3 is estimated to be only 32%[16], meaning that 2 out of 3 projects reaching this phase will be abandoned. This points to severe deficiencies in the predictive power of preclinical research.

*Horizon Europe should ensure that **funded projects include a rigorous innovation management plan**, covering various necessary steps **leading to market access** and leveraging the following expertise: intellectual property, regulatory requirements, health technology assessment, ethics, trial protocol and management methodology. Such criteria would also imply **the involvement of a wide range of stakeholders in project consortia.***

Each medical ERIC has addressed this issue by developing accessible solutions for researchers. ECRIN offers a unique service called "ECRIN-On-Board[17]", aiming to improve the quality of EU funding applications through early support on the clinical trial protocol and the logistical/operational aspects of project design. EATRIS provides complete Innovation Management support, as well as their translational optimisation service[18], which assesses the translational feasibility and potential of research projects. By providing feedback on issues such as medical need, market and pipeline overview, regulatory pathway, intellectual property and translational tools, investigators can optimise their plans according to the realities of the development pipeline. Additionally, services like the BBMRI-ERIC Directory, Locator and Negotiator can help researchers to find the right samples to test diagnostics, biomarkers and treatments throughout the development process[19].

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[12] https://zenodo.org/record/825054#.WzNCFtIzYuU
[13] DiMasi JA, Grabowski HG, Hansen RW (2016) Innovation in the pharmaceutical industry: New estimates of R&D costs; Journ Health Economics, 47; 20-33
[14] S. Morgan, P. Grootendorst, J. Lexchin, C. Cunningham, D. Greyso; The cost of drug development: A systematic review; Health Policy, Volume 100, Issue 1, 2011, Pages 4-17.
[15] DiMasi, J. A., Feldman, L. , Seckler, A. and Wilson, A. (2010), Trends in Risks Associated With New Drug Development: Success Rates for Investigational Drugs. Clinical Pharmacology & Therapeutics.
[16] Hay et al, Clinical development success rates for investigational drugs (2014) Nat. Biotech. 32, 40–51
[17] http://www.ecrin.org/activities/ecrin-on-board
[18] https://eatris.eu/solutions/eatris-inside-for-funding-applications/
[19] http://www.bbmri-eric.eu/services/directory/

Who are we?

BBMRI-ERIC (Biobanking and BioMolecular resources Research Infrastructure - European Research Infrastructure Consortium)

BBMRI-ERIC is the world largest biorepository of human samples (such as blood, tissues, cells or DNA, and associated clinical and research data), connecting more than 500 biobanks from 19 EU countries. Its mission is to facilitate research on human samples for personalised medicine, while keeping the highest scientific standards and, most importantly, preserving patients' and citizens' privacy. BBMRI-ERIC provides services to academia and industry to develop better treatments, test diagnostic tools and advance biomedical research. It has been a part of 42 Horizon 2020 calls with an overall success rate of 26%. BBMRI-ERIC is composed of 19 national nodes, that support biobanking at the local level, and a European headquarters, based in Graz, Austria.

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EATRIS (European Research Infrastructure for Translational Medicine)

EATRIS aims to create a global framework preventing research waste by supporting the dissemination of good research practices, based on quality, reproducibility and standardisation. EATRIS helps academia and industry de-risk and add value to their drug, vaccine or diagnostic development programmes. We do this by providing fast, tailored access to cutting-edge enabling technologies and expertise in translational research, focusing on preclinical and early clinical development of drugs, vaccines and diagnostics. Via our central hub in Amsterdam, users can access the vast array of clinical expertise and high-end facilities that are available within the 80+ top-tier academic centres across 12 countries in Europe. Solutions are provided in the fields of advanced therapy medicinal products, biomarkers, imaging and tracing, small molecules and vaccines.

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ECRIN (European Clinical Research Infrastructure Network)

ECRIN-ERIC supports the planning, set-up and operational management of multinational clinical research in Europe, providing access to patients and medical expertise throughout Europe. ECRIN addresses various challenges and obstacles, including infrastructure interoperability, regulatory and ethical requirements, multinational trial management and funding issues, by offering researchers support to prepare and implement multinational studies. Support areas include advice in study planning and in the preparation of funding applications, protocol peer-review, and operational services to multinational trial management. This is based on its distributed organization with expert staff located in each Member and Observer country, and on trial management tools developed by ECRIN. ECRIN participates in 40 H2020-funded projects, and its portfolio includes 50 multinational trials, with an average of seven countries per trial.

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