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PART2

LANDSCAPE ANALYSIS - SECTION1

HEALTH & FOOD

HEALTH & FOOD

KEY MESSAGES

The Health & Food RIs landscape is consolidating firmly in the European Research Area with now 10 Landmarks and 6 Projects covering the vast remit of health, agri-food and the bioeconomy.

To generate readiness to meet current challenges and demands, the Health & Food RIs need to continue cementing their efforts and connecting between them using their different competences and technologies at the service of the user community.

Gaps in the Health & Food landscape can be identified at many levels and it will also be important to connect infrastructure efforts with other domains, as significant innovations and new developments often occur at the boundaries of research areas.

In the field of data, further efforts are required to promote and facilitate the interaction between domains and to avoid fragmentation of the data continuum.

There is a broad consensus that future competitiveness in a globalised knowledge economy depends on research capability. Research Infrastructures (RIs) in the Biological, Agri-Food and Medical Sciences – i.e. Health & Food – continue to establish themselves as research, innovation and skills hubs and as a motor for economic impact. This is reflected in increasing levels of industrial access to RIs, and in their European and global positioning.

The economic impact of investments in large-scale biomedical research, such as the 3.75 billion € investment in the Human Genome Project, has spurred an estimated 900 billion € in economic growth, i.e. a 178-fold return on investment[1]. The bioeconomy on the other hand is estimated to be worth at least 2 trillion € in the EU[2]. The arrival of the digital age allows sharing and collective working on a large and distributed scale. Health & Food RIs are key catalysers of progress and change in this new age. The increasing level of sophistication in instrumentation, tools and techniques means that even very large institutions or laboratories cannot provide and maintain access to all services relevant to the field in question, hence services need to be more specialised and distributed. Distributed RIs offer an interdisciplinary set of skills, complemented by disciplines outside the Biological, Agri-Food and Medical sciences, and are well positioned to address the challenges facing our society today, which see no countries, boundaries or disciplines.

ESFRI has been instrumental and influential in the co-ordination of national decision-making and investment in European RIs in Health & Food. The landscape continues to evolve and it is important to ensure its ability and agility to respond to current and future demands. Much effort has been invested nationally and at EU level in identifying and establishing the current RIs in the ESFRI Roadmap (see **Figure 1**). These key infrastructures are at different stages in their implementation, providing access to a range of key services and giving much visibility to the Health & Food landscape.

Health & Food RIs are also taking an increasing role internationally. The Report of the Group of Senior Officials on Global Research Infrastructures[3] lists the **ESFRI Landmarks BBMRI ERIC** (Biobanking and BioMolecular Resources Research Infrastructure), **ELIXIR** (A distributed infrastructure for life-science information) and **INFRAFRONTIER** (European Research Infrastructure for the generation, phenotyping, archiving and distribution of mouse disease models) as Research Infrastructures of Global Interest recognising their global leadership.

There has been continued progress towards alignment of the Health & Food landscape with the national roadmaps. This is contributing to increased efficiency between existing RIs and will help consolidate existing and new RIs. The landscape requires sustained effort to complement with new RIs, to maximise current services, and to cement new functionalities, integration and interactions with the relevant fields. The Health & Food landscape considers the current and future challenges in Europe, notably in the provision of healthcare and sustainable and healthy food in the context of a changing cli-

1. Economic Impact of the Human Genome Project. Battelle Technology Partnership Practice for United for Medical Research – Tripp, S. & Grueber, M., 2011 https://bit.ly/2NaAzbQ

2. A Bioeconomy Strategy for Europe, 2012 http://ec.europa.eu/research/bioeconomy/

3. GSO Progress Report, 2017 https://ec.europa.eu/research/infrastructures/pdf/gso_progress_report_2017.pdf

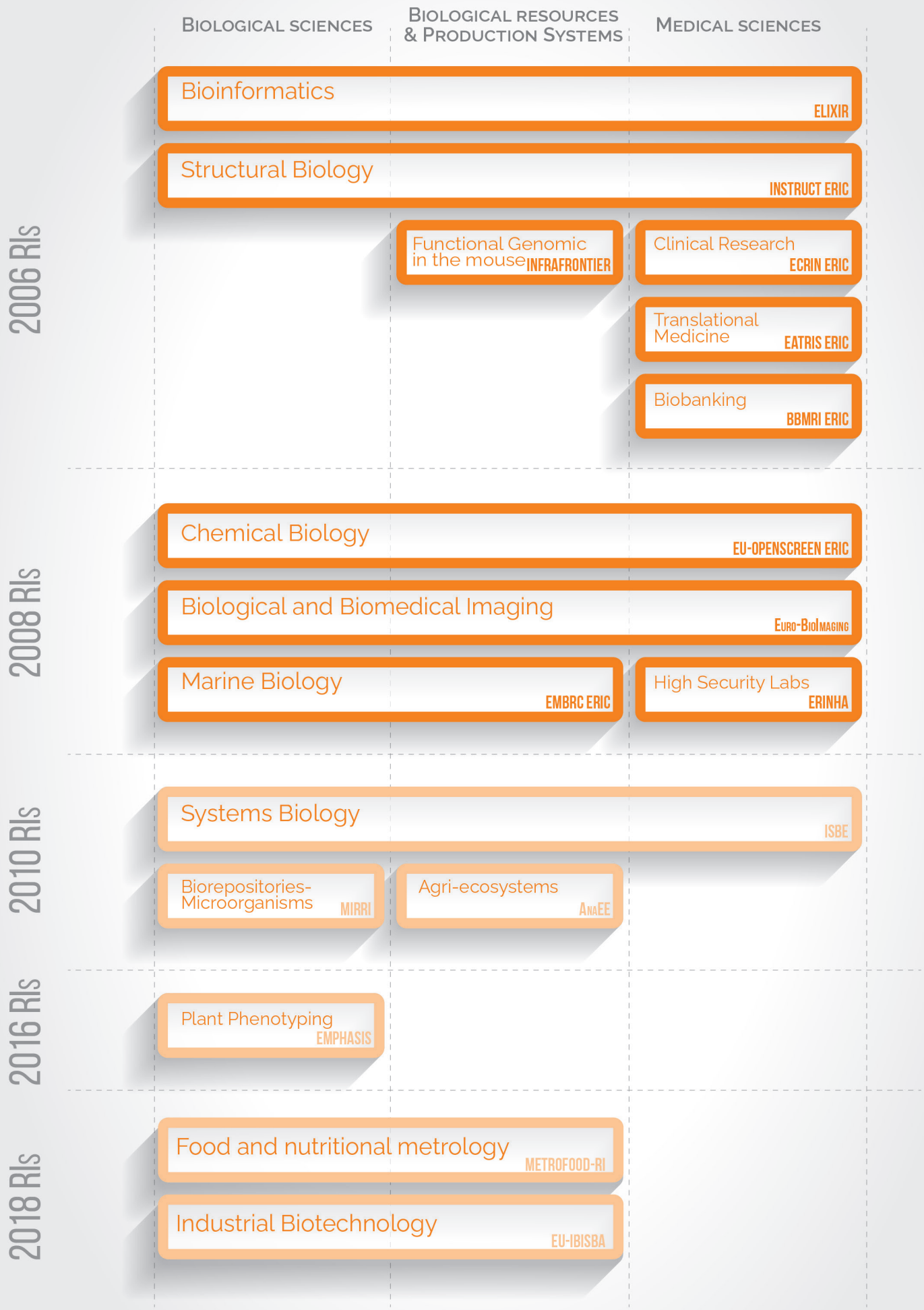

FIGURE 1.
Health & Food Research Infrastructures in ESFRI Roadmap 2018

mate and limited land availability. In order to generate readiness to meet the challenges and demands, the Health & Food RIs need to continue connecting with each other and with the entire scientific landscape, using their different competences and technologies at the service of the user community. Health & Food RIs[4] provide complementary and synergistic infrastructure facilities (see **Figure 2**), and contribute to building the ERA by:

- providing pan-European open access to cutting-edge technology platforms for academia and industry;
- enabling researchers to find new solutions to meet the major societal challenges they face collectively, including the health of the ageing population and the environmentally sustainable supply of affordable and nutritious food;
- promoting interdisciplinary and excellent research in Biological, Agri-Food and Medical Sciences across Europe, alignment and standardising the European research landscape and reducing fragmentation;
- promoting interdisciplinary connections with other domains in Energy, the Environment, Physical Sciences & Engineering, and in Social & Cultural Innovation;
- rapidly translating findings from basic science to new applications in Biology, Agri-Food and Medicine;
- delivering synergies and highly interoperable research processes, creating seamless value chains;
- identifying and accelerating the development and integration of technologies into the infrastructures to meet emerging needs;
- generating opportunities to maximise the competitiveness of Europe's knowledge-based industry and the bioeconomy – e.g. the agricultural, pharmaceutical, biotechnology and food industries, plus advanced equipment manufacturers, as well as development and utilisation of intellectual property;
- providing training and education to current and future Research Infrastructure professionals;
- attracting and retaining world-leading scientists within the ERA.

4. Biological and Medical Sciences Thematic Working Group Report, 2010
http://ec.europa.eu/research/infrastructures/pdf/bms_report_en.pdf

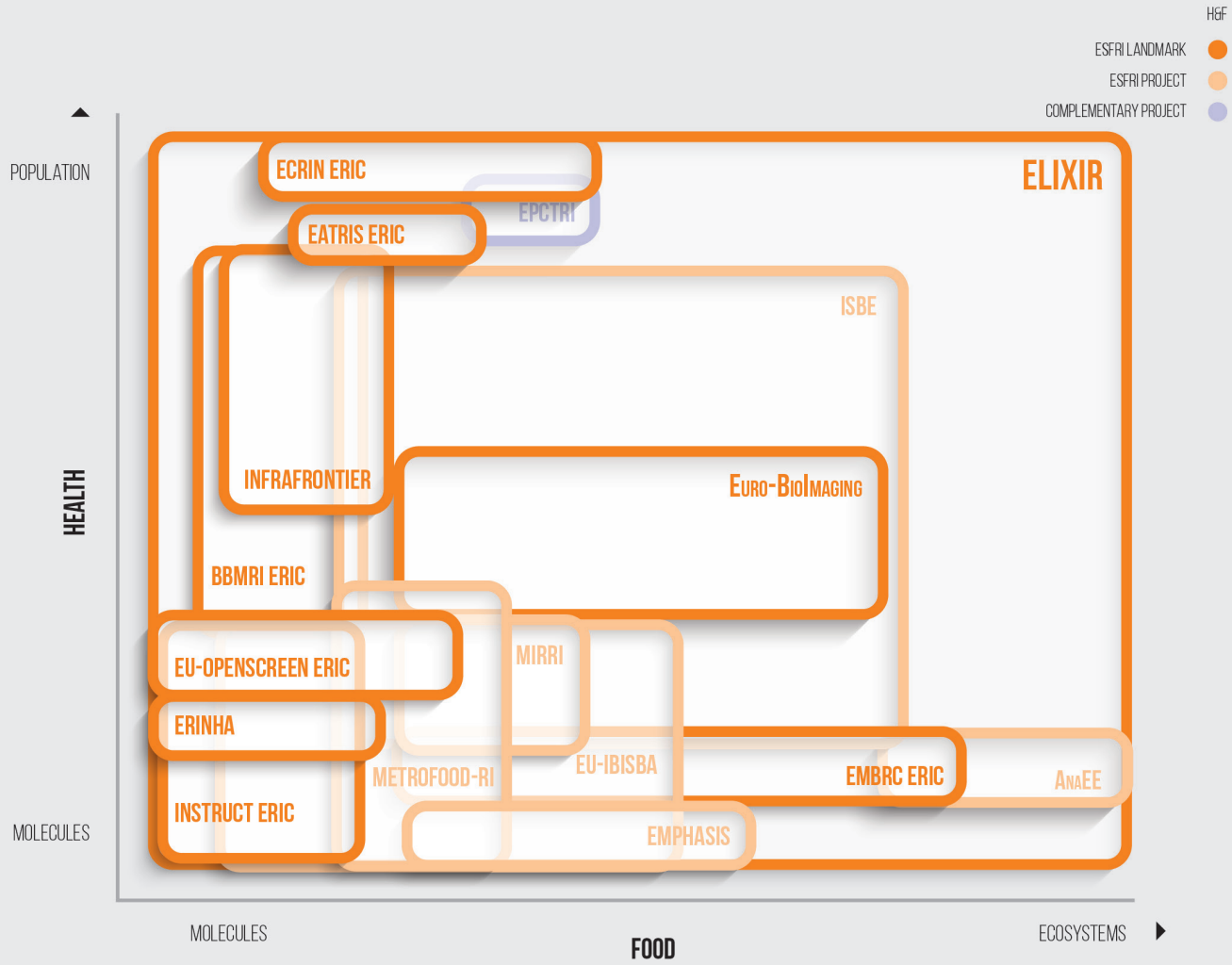

FIGURE 2.
The indicative position of ESFRI RIs relative to the different levels of organisation in the Health & Food domain

THE HEALTH CHALLENGE

There is a rising demand for health care in Europe and worldwide, brought by an ageing population with a complex disease-pattern and chronic diseases. Modern lifestyles further add to the costs, e.g. through increasing incidence of disease like diabetes type 2, cancer and infectious diseases. Moreover, changes in climate are likely to affect human health in Europe particularly in older people and those with chronic diseases (IPCC, 2014). Increase in the incidence of mental health problems also needs to be addressed. Developing relevant and effective prevention, screening, early diagnosis, treatment and rehabilitation, research questions call for research which is capable to use complex inter- and cross-disciplinary research models, technologies, and bridges between scientific disciplines and society[5,6,7]. The next generation will have demands on the health and care community based on all information which can be accessed. This combined with an overall improved economic situation where tomorrow's elderly will need to get the most effective treatment, prediction of illness and homecare. This is one societal challenge to be addressed and communicated. There is a need to continue bringing together leading healthcare companies across multiple industry sectors, public and private research centres, and top universities, to accelerate entrepreneurship and innovation in healthy living and active ageing for the benefit of all EU citizens[8].

We are in a transition phase moving away from a *one-size-fits-all* approach into customised health care that is tailored to the needs of the individual. Personalised medicine focuses on the patients based on their individual clinical characterization. Precision medicine focuses on identifying which approaches will be effective for which patients based on genetic, environmental, and lifestyle factors. This transition towards customised health care is data- and knowledge-driven. The challenge of data- and knowledge- collection, management and stewardship for precision medicine is already beginning to be met by pan-European infrastructures like the **ESFRI Landmarks ELIXIR, BBMRI ERIC, INFRAFRONTIER** and others (see **Figure 3**), – including ethical, legal and social implications. For proper storage and smart retrieval of these data and knowledge, ICT for health is indispensable. Data relevant to precision medicine are not only generated in the laboratory and clinic. Citizens and patients are increasingly taking advantage of social media and app technologies to share information about their own health and lifestyle. Data shared by patients have already been

5. Advice For 2016/2017 of the Horizon 2020 Advisory Group For Societal Challenge 1. Health, Demographic Change And Wellbeing, 2014
http://ec.europa.eu/transparency/regexpert/index.cfm?do=groupDetail.groupDetailDoc&id=15073&no=1

6. Shaping Europe's Vision for Precision Medicine, 2015
http://www.permed2020.eu/_media/PerMed_SRIA.pdf

7. The Precision Medicine Initiative Cohort Program – Building a Research Foundation for 21st Century Medicine, 2015
https://acd.od.nih.gov/documents/reports/DRAFT-PMI-WG-Report-9-11-2015-508.pdf

8. EIT Health
https://www.eithealth.eu/

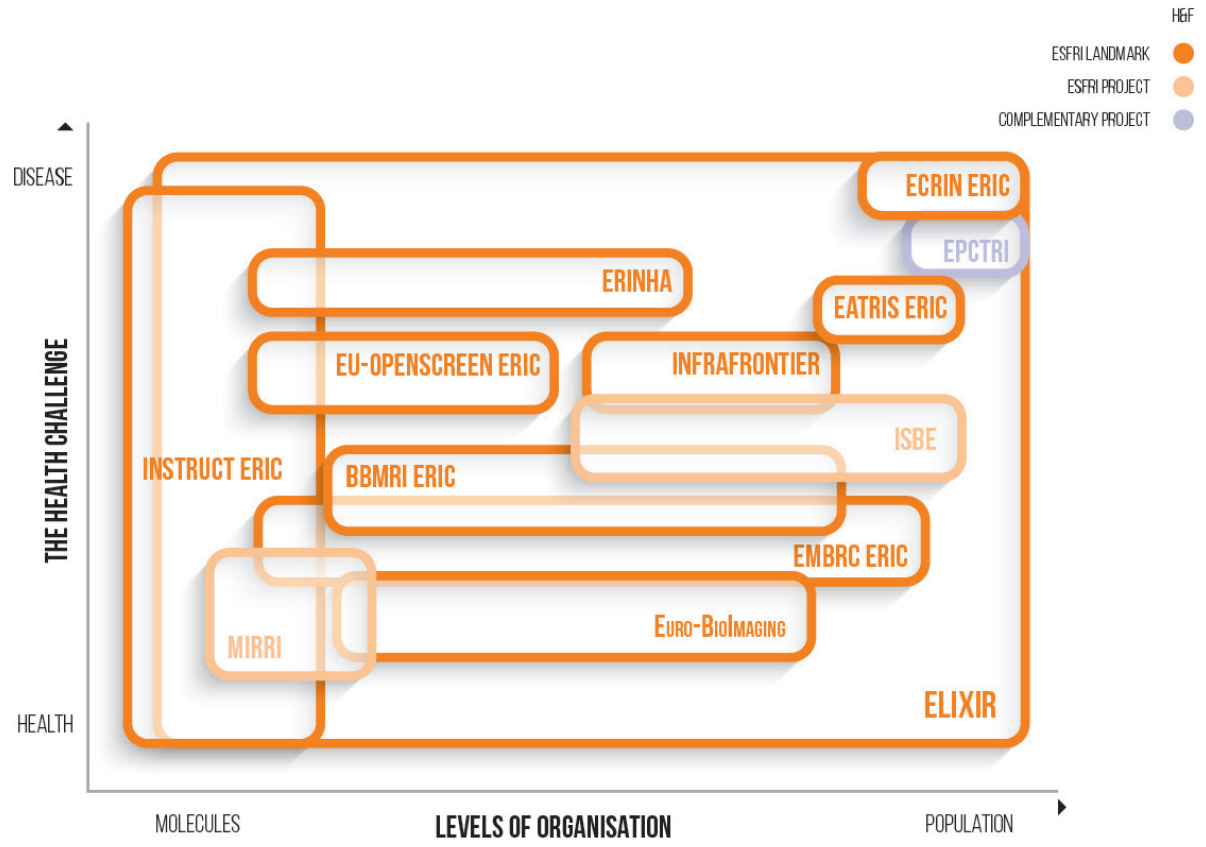

FIGURE 3.
The indicative position of ESFRI Research Infrastructures relative to the different levels of organisation in the Health domain

used effectively for research purposes and it is apparent that this sort of citizen-led collaboration can serve to accelerate clinical research.

The development of increasingly tailored interventions will require smooth translation – the **ESFRI Landmark EATRIS ERIC** (European Advanced Translational Research Infrastructure in Medicine) – and new clinical trial designs to take account of the shift in focus from population to well-defined cohorts of even individuals – the **ESFRI Landmark ECRIN ERIC** (European Clinical Research Infrastructure Network) and the complementary project EPCTRI (European Paediatric Clinical Trial Research Infrastructures), which is focused on paediatric clinical trials. The experience can be extrapolated to other designs involving relatively few patients, e.g. rare diseases. The EU launched a Consultative Group on the European Joint Programme (EJP) for Rare Diseases, in which the **ESFRI Landmarks EATRIS ERIC** and **ECRIN ERIC**, and the complementary project EPCTRI, are actively participating. The aim is to consolidate the transnational research on rare diseases through existing European platforms, and in the framework of the Horizon 2020 work programme 2018-2020, under Societal Challenge 1 - Health, Demographic change, and Well-being. Customised health-care is becoming one of the highly valued new possibilities for science and society. New threats, including pandemics, and exacerbation of diseases thought to be already eradicated, require the developments of innovative treatments and new strategies for the design of new drugs and potent vaccines – the **ESFRI Landmark INSTRUCT ERIC** (Integrated Structural Biology Infrastructure). Improved health-care will inevitably face the problem of the need for new therapies requiring bioinformatics – the **ESFRI Landmark ELIXIR**; experimental analysis of targets – the **ESFRI Landmark INSTRUCT ERIC**; medicinal chemicals and new biologicals – the **ESFRI Landmarks EU-OPENSCREEN ERIC** (European Infrastructure of Open Screening Platforms for Chemical Biology) and **INSTRUCT ERIC;** an integrated approach to modelling disease – the **ESFRI Project ISBE** (Infrastructure for Systems Biology Europe); and state-of-the-art imaging technologies – the **ESFRI Landmark Euro-BioImaging** (European Research Infrastructure for Imaging Technologies in Biological and Biomedical Sciences). In the case of emerging infectious diseases, as recently demonstrated by the Ebola outbreak, high-containment infrastructures will be crucial for new research – category 4 containment, the **ESFRI Landmark ERINHA** (European Research Infrastructure on Highly Pathogenic Agents) – including contained characterisation methods (category 3 and 4 electron microscopy). Important underpinning bioscience developments, such as the Human Cell Atlas, are in preparation. The Human Cell Atlas is an ambitious international programme with active participation by European countries, aiming to facilitate a comprehensive reference maps of all human cells as a basis for understanding human health and diagnosing, monitoring and treating disease[9,10,11,12,13].

9. The Human Cell Atlas
https://www.humancellatlas.org/

10. The 2015 Ageing Report
http://ec.europa.eu/economy_finance/publications/european_economy/2015/pdf/ee3_en.pdf

11. The Data Mapping Project
http://www.jpi-dataproject.eu/

12. EIT Health
https://www.eithealth.eu/about

13. Towards Cleaner Air Scientific Assessment Report 2016
http://www.unece.org/index.php?id=42861

THE FOOD CHALLENGE

The global demand for food is predicted to increase 50% by 2030 and 100% by 2050. In many European countries, the growth trends of the yields of major crops, especially wheat, have declined over the past two decades and the variability of crop yields has increased as a consequence of extreme climatic events, such as the summer heat of 2003, which led to 36 billion € economic losses. FAO's 2016 report on the State of Food and Agriculture estimates decrease in yield of major European crops like wheat, maize and soybean under different climate scenarios. We need to produce more food whilst considering the influence of a changing climate, by increasing crop yield, and the efficiency, resilience and sustainability of the food chain, i.e. more product for less water, energy and chemical inputs. Substantial improvements with regard to livestock production are also needed, including new or more efficient strategies for preventing and managing livestock pathogens and the impact of antimicrobial resistance. But food security is also about improving nutritional and health benefits of foods, and making it accessible and affordable, globally, also minimising food waste. The UN sustainable development goals set food waste reduction targets of the following "halve per capita global food waste at the retail and consumer level, and reduce food losses along production and supply chains by 2030". Additionally, the Paris Agreement in 2015 recognised the important role of food production system in a changing climate and offers many opportunities in the food and farming sectors to limit the global temperature increase to well below 2 degrees.

The food system is by far the largest industrial sector in Europe in terms of turnover, value added and employment. In 2014, the activities with the strongest growth were agriculture, forestry and fishing (2.8%) and food services (2.1%) among others. An innovative bioeconomy in support of a *green growth* strategy that combines economic growth, natural resource preservation, highly efficient resource utilisation in well integrated value chains and greenhouse gas reduction is necessary. The bioeconomy is estimated to be worth at least 2 trillion € in the EU and employing around 22 million people. The objective is to secure sufficient supplies of safe, healthy and high quality food and other bio-based products, by developing resource-efficient primary production systems, fostering related ecosystem services and the recovery of bio-diversity, alongside competitive and low carbon supply chains[14,15,16,17,18,19,20,21,22]. The food system fits in the concept of circular economy as a regenerative system that aims to preserve and enhance natural capital, optimises resource yields, and minimises system risks. Embedded in the framework of sustainable development, the goal is to produce goods and services while reducing the consumption and wastage of raw materials, water and energy sources[23]. The *blue economy* is another area with great potential for innovation and growth, representing roughly 5.4 million jobs and generating a gross added value of almost 500 billion € a year[24]. There is a need to continue developing the marine biotechnology pipeline towards Blue Growth, and deliver the long term strategy to support sustainable growth in the marine and maritime sectors[25].

Important steps have been taken with G7 Future of the Seas and Oceans Initiative[26], COP21[27] and FOOD 2030. The realisation of these, among other large initiatives, will require new collaborations between Research Infrastructures and perhaps new configurations and approaches.

Europe is well placed to address these issues. The European RIs currently on the Roadmap constitute the starting point to achieve this ambitious goal for Europe: the **ESFRI Project AnaEE** (Infrastructure for Analysis and Experimentation on Ecosystems) on experimental manipulation of managed and unmanaged terrestrial and aquatic ecosystems, the **ESFRI Project EMPHASIS** (European Infrastructure for Multi-scale Plant Phenomics and Simulation), the **ESFRI Landmark EMBRC ERIC** (European Marine Biological Resource Centre) on marine ecosystems and biological resources, the **ESFRI Landmark ICOS ERIC** (Integrated Carbon Observation System, ENV) on high precision monitoring of greenhouse gas fluxes, other RIs from the ENV domain, the **ESFRI Project MIRRI** (Microbial Resource Research Infrastructure) on microorganisms-oriented services applied to biotechnology and food production, the **ESFRI Landmark Euro-BioImaging** on integrating imaging technologies and services (with links to crop phenotyping), the **ESFRI Landmark ECRIN ERIC** on clinical trials and nutritional trials, the **ESFRI Landmark INSTRUCT ERIC** on the use of structural biology to support plant and animal sciences, the **ESFRI Project ISBE** on integrated approach to food systems, and the **ESFRI Landmark ELIXIR** on life sciences large-scale data and knowledge management – applied to agriculture and bioindustries – and their links to other multidisciplinary RIs (see **Figure 4**).

14. How to feed the world in 2050. Food and Agriculture Organization of the United Nations (FAO), 2009 http://www.fao.org/fileadmin/templates/wsfs/docs/expert_paper/How_to_Feed_the_World_in_2050.pdf

15. Climate Change 2014, Synthesis Report - IPCC, 2014 http://www.ipcc.ch/report/ar5/syr/

16. A European science plan to sustainably increase food security under climate change. Soussana et al. Global Change Biology 18 (11), p. 3269–3271, 2012

17. European Statistics (Eurostat) - European Commission, 2008 http://ec.europa.eu/eurostat

18. The Joint Programming Initiative on Agriculture, Food Security and Climate Change (FACCE-JPI) https://www.faccejpi.com/

19. Joint Programming Initiative – A Healthy Diet for a Healthy Life (JPI-HDHL) https://www.healthydietforhealthylife.eu/

20. A Bioeconomy Strategy for Europe, 2012 http://ec.europa.eu/research/bioeconomy/index.cfm

21. Sustainable Agriculture, Forestry and Fisheries in the Bioeconomy. A Challenge for Europe. 4th SCAR Foresight Report, 2015 https://ec.europa.eu/research/scar/pdf/ki-01-15-295-enn.pdf

22. Sustainable Development Goals 17 Goals to Transform the World https://www.un.org/sustainabledevelopment/sustainable-development-goals/

23. Circular Economy European Summit http://www.circulareconomysummit.com/

24. Maritime affairs, Integrated maritime policy – Blue Growth https://ec.europa.eu/maritimeaffairs/policy/blue_growth_en

25. The European Marine Biological Research Infrastructure Cluster: An Alliance of European Research Infrastructures to Promote the Blue Bioeconomy - Grand Challenges in Marine Biotechnology, pp 405-421, Piña M. et al., 2018 https://doi.org/10.1007/978-3-319-69075-9_10

26. G7 Future of Seas and Oceans http://www.g7italy.it/sites/default/files/documents/ANNEX 1_WG Future of the Seas and Oceans.pdf

27. COP21 http://www.cop21paris.org/

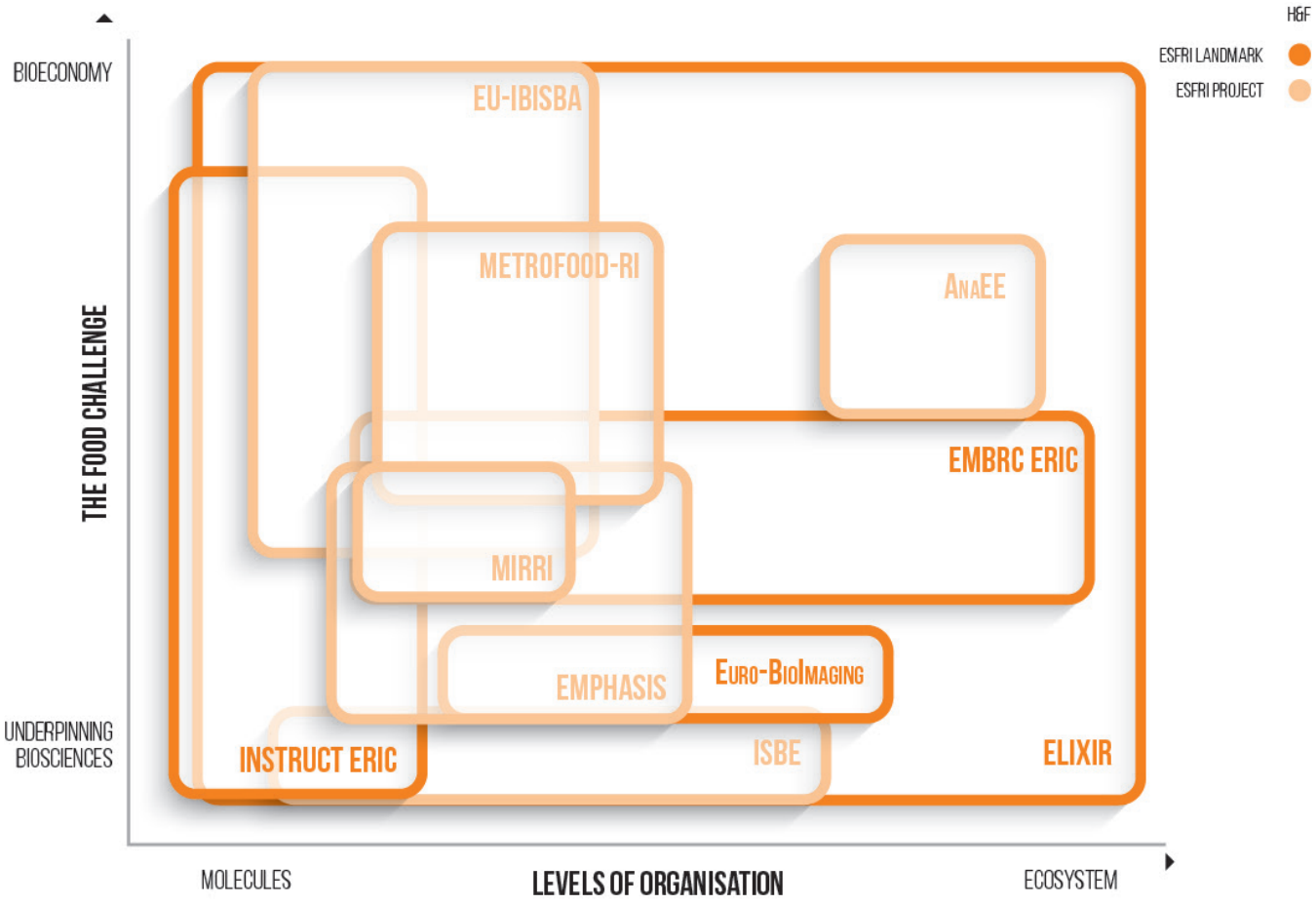

FIGURE 4.
The indicative position of ESFRI Research Infrastructures relative to the different levels of organisation in the Food domain

THE FAIR DATA REVOLUTION

The Open Data agenda has been driven steadily by the Health & Food distributed infrastructures in collaboration with relevant stakeholders. DNA sequencing technologies have revolutionised the life sciences, from basic biological research right through to biomedical, biotechnology and agri-food applications. High-throughput sequencing technologies now produce billions of bases of nucleotide data per experiment, at a low cost. There are now more opportunities to cross-fertilise different omics platforms, data sets and informatics. Imaging technology is producing vast amounts of data revealing life in unprecedented detail. Structural investigation technologies are also accumulating data at a rate in excess of Moore's law. Cloud computing is estimated to reach a total cumulative gain of 940 billion € in the period 2015-2020. The life science sector is an intensive user of High Performance Computing and it is expected this will increase further[28,29,30]. The data and knowledge generated are contributing to extend the boundaries of frontier and applied research, and to respond to the Health & Food challenges. This will increase opportunities for all stakeholders to be part of the landscape and build competencies, regardless of whether they have the RI in their own country.

ESFRI Health & Food RIs are at the heart of realising the data revolution, by providing pan-European access to the specialised research services and data, suitably open for innovation by industry. A growing number of European and National RIs and projects are established following the EC recommendation on access to and preservation of scientific information[31]. Some e-Infrastructure projects – i.e. OpenAire – offer infrastructure for researchers to support them in complying with the EC Open Access pilot and the ERC Guidelines on Open Access. The European Charter for Access to RIs[32] sets out non-regulatory principles and guidelines for defining access policies for RIs. The Charter promotes interaction with a wide range of social and economic activities, including industry and public services, to maximise the return on investment in RIs and to drive innovation, competitiveness and efficiency. A number of e-RI projects address Data Management Policy in coordination and synergy with Health & Food RIs[33], e.g. BioMedBridges Charter for Data Sharing[34], or in the ERIC process. FAIRDOM[35] is an internationally sustained service to manage project data from instrument to publication since 2008. Establishing good data and model management practices ensures that data and models are findable, accessible, interoperable and reusable (FAIR). The high-level FAIR Guiding Principles[36] were established to precede implementation choices, and do not suggest any specific technology, standard, or implementation-solution. They act as a guide to data publishers and stewards to assist them in evaluating whether their particular implementation choices are rendering their digital research artefacts Findable, Accessible, Interoperable, and Reusable. It is anticipated that these high level principles will enable a broad range of integrative and exploratory behaviours, based on a wide range of technology choices and implementations. Indeed, many repositories are already implementing various aspects of FAIR using a variety of technology choices. ESFRI Health & Food RIs are playing a key role in the promotion and implementation of these principles. In addition, life sciences research relies extensively upon a set of core resources that archive, curate, integrate, analyse, and enable ready access to data, information, and knowledge generated worldwide by hundreds of thousands of researchers. The sustainability of core data resources is being discussed internationally, with the **ESFRI Landmark ELIXIR** playing a key role[37].

The FP7 BioMedBridges and the H2020 CORBEL projects represent a successful joint effort of Health & Food RIs to develop common approaches and standards for data integration in the biological, medical, translational and clinical domains. The **ESFRI Landmark INSTRUCT ERIC** has developed ARIA, a platform for harmonised user access to biological and medical technologies, biological samples and data services required by cutting-edge research. Within CORBEL, the ARIA platform has been further optimised for integrated access to multiple RIs. The current global research data landscape is highly fragmented, by disciplines or by domains, from oceanography, life sciences and health, to agriculture, space and climate. Health & Food RI experts participate actively in the Research Data Alliance[38], a high profile international initiative - over 2.500 membership from 92 countries - aiming at building the social and technical bridges across these areas that enable open sharing of data. Health & Food RIs are also contributing to shape the European Open Science Cloud (EOSC), an EC-led initiative aiming at interconnecting existing Research Infrastructures to offer European researchers and professionals a virtual environment to store, share and re-use their data across disciplines and borders. EOSC will be underpinned by the European Data Infrastructure, deploying the high-bandwidth networks, large scale storage facili-

28. Biology: The big challenges of big data. Marx, V. Nature 498, 255-260, 2013

29. Quantitative Estimates of the Demand for Cloud Computing in Europe and the Likely Barriers to Uptake, 2012 http://ec.europa.eu/information_society/newsroom/cf/dae/document.cfm?doc_id=1115

30. e-IRG White Papers, 2014 http://e-irg.eu/white-papers

31. Commission Recommendation, 2012. https://bit.ly/20kxYvB

32. European Charter for Access to RIs, 2015 https://ec.europa.eu/research/infrastructures/pdf/2016_charterforaccessto-ris.pdf

33. Towards coordination of international support of core data resources for the life sciences. Anderson et al., 2017 https://www.biorxiv.org/content/early/2017/04/27/110825

34. BioMedBridges, Principles of data management and sharing at European RIs. 2014. https://zenodo.org/record/8304/files/BioMedBridges-principles-of-data-management-and-sharing-at-RIs_.pdf

35. FAIRDOM https://www.fairdomhub.org/

36. The FAIR Guiding Principles for scientific data management and stewardship https://www.nature.com/articles/sdata201618

37. Data management: A global coalition to sustain core data https://www.nature.com/articles/543179a.

38. The Research Data Alliance is supported by The Australian Commonwealth Government through the Australian National Data Service supported by the National Collaborative Research Infrastructure Strategy Program and the Education Investment Fund (EIF) Super Science Initiative, the European Commission through the RDA Europe project funded under the 7th Framework Program and the United States of America through the RDA/US activity funded by the National Science Foundation and other U.S. agencies.

ties and super-computer capacity necessary to effectively access and process large datasets stored in the cloud. The **ESFRI Landmarks ELIXIR**, **ECRIN ERIC, INSTRUCT ERIC** and **BBMRI ERIC** are participating actively in EOSC Pilot. The EOSC's Stakeholder Forum in November 2017 attracted all Health & Food RIs to help define EOSC future. A group of EU member states is preparing the GO FAIR initiative, which is a proposal for the practical implementation of the EOSC initiated in the life sciences domain by the ELIXIR node DTL in The Netherlands among others. The current H2020 WP2018-20 for Research Infrastructures includes a call for cluster projects targeted to ESFRI projects and landmarks in all domains: Biomedical Sciences, Environment and Earth Sciences, Physics and Analytical Facilities, Social Sciences and Humanities, Astronomy, Energy. Research Infrastructures can only participate in one cluster. Further efforts may be required to promote and facilitate the interaction between domains and to avoid fragmentation of the data continuum.

The Open Access concept is widely accepted and promoted by ESFRI Landmarks in Health & Food. The **ESFRI Landmark BBMRI ERIC** and its Common Service ELSI aim at facilitating and supporting cross-border exchanges of human biological resources and data attached for research uses, whilst giving proper consideration of ethical, legal and social issues. The **ESFRI Landmark INSTRUCT ERIC** has adopted a data policy that specifically encourages its users to make their data open and mandates the development of the required tools. The **ESFRI Landmark ELIXIR**, together with the **ESFRI Landmark CLARIN ERIC** (Common Language Resources and Technology Infrastructure, SCI) and **ESFRI Landmark DARIAH ERIC** (Digital Research Infrastructure for the Arts and Humanities, SCI), in the social sciences and humanities, and the DASISH cluster project, have endorsed the eduGAIN Data Protection Code of Conduct. Health & Food RIs are actively managing all aspects related to the implementation of the new General Data Protection Regulation (GDPR), effective from May 2018. The GDPR applies to both automated personal data and to manual filing systems where personal data are accessible according to specific criteria.

INTERCONNECTED SERVICES AND CAPABILITIES

The Health & Food RI landscape is made up of a vast number of national infrastructures interconnected at different levels. Many of the framework programme Integrating Activities (IA) have provided the foundation and primary integration for more complex RIs, as communities mature and the case for higher integration and connection is refined.

For instance, the **ESFRI Landmark INSTRUCT ERIC** integrates a series of IA projects of specialised structural technologies and tools, i.e. X ray diffraction, NMR, EM and Mass Spec (Bio-NMR, BioStructX, PrimeX, PCUBE) pushing beyond the horizon of each individual technology. The **ESFRI Project EMPHASIS** integrates IA projects EPPN and EPPN2020, facilitating access to 31 key plant phenotyping installations, developing novel technologies and methods for environmental and plant measurements, tools for statistical analysis and information systems, and integrating phenotyping facilities and users in the EU and internationally. The combination of research capability and capacity of ESFRI RIs and IAs enhances the landscape and accelerates the transfer of data and technologies into services and innovation.

The Health & Food RIs constitute an advanced level of integration at pan-EU scale, bringing together facilities, services and resources for research, and taking them to a new level of expertise and synergy. ESFRI in its incubator role has enabled the current Health & Food RIs to significantly change the infrastructure landscape: they are in a unique position to offer complementary or sequential processes and services in different fields. This is the model of the **ESFRI Landmarks INFRAFRONTIER**, **INSTRUCT ERIC, EATRIS ERIC** and **ECRIN ERIC** together with EPCTRI**,** in association with the **ESFRI Landmarks BBMRI ERIC** and **ELIXIR**. In early stage drug discovery, the **ESFRI Landmarks EU-OPENSCREEN ERIC** and **INSTRUCT ERIC** provide a platform for identifying candidate compound hits for target pipelines; the **ESFRI Landmark INFRAFRONTIER** provides animal models to test hypotheses preliminary to human testing; the **ESFRI Landmarks INSTRUCT ERIC** and **EATRIS ERIC** provide the translational pre-clinical and early clinical research facilities; and the **ESFRI Landmark ECRIN ERIC** provides the clinical infrastructure for the clinical research on diagnostic and therapeutic procedures and clinical trials of drugs and devices in patients. The Complementary Project EPCTRI, offers a facility to deliver clinical trials involving children with uniform standards across Europe. EPCTRI and the **ESFRI Landmark ECRIN ERIC** have aligned their efforts at strategic and operational level, for mutual benefit. The H2020-funded project PedCRIN is helping to consolidate these efforts. It is expected that similar integrated service pipelines will be established in other areas of the Health & Food landscape, e.g. marine biotechnology, industrial biotechnology, and sustainable agri-food systems, where the **ESFRI Landmark EMBRC ERIC**, and the **ESFRI Projects AnaEE, EMPHASIS, EU-IBISBA** (Industrial Biotechnology Innovation and Synthetic Biology Accelerator), **METROFOOD-RI** (Infrastructure for promoting Metrology in Food and Nutrition) and **MIRRI** will play a significant role.

Integrating technologies at different levels of complexity is allowing RIs to tackle problems using a systems approach. The **ESFRI Project ISBE** is an example of a RI with a role in integrating life sciences technologies, data and services between the Health & Food RIs, with complementarities with ESFRI Landmarks and Projects, like the **ESFRI Landmark ELIXIR.** An example of integration of services at thematic level can be that for diagnosing rare diseases, as critical amount of data is gathered and shared from different countries in Europe that otherwise would not be available. Meta- or global infrastructures with a thematic and/or a technological focus are key elements of the landscape.

GAPS, CHALLENGES AND FUTURE NEEDS

There are some significant gaps to be filled and connections to be enabled across the pan-European landscape of infrastructures in Health & Food. There is a need for a pan-EU approach on food and nutrition as well as in sustainable agriculture and bio-economy, building a natural link between the two complex medical and agriculture fields. Gaps can be identified at many levels and in order to complete the landscape, it will also be important to connect infrastructure efforts within Health & Food and with other domains. Significant innovations and new developments often occur at the boundaries of research areas, and Health & Food Strategic RIs have already established effective connections between them and across other ESFRI domains. As the landscape keeps evolving, new connections will and need to be made; ESFRI Landmarks and Projects in all domains have a key role to play as a driver in promoting and facilitating effective and fruitful connections, as well as in supporting the ERA.

These new connections need to be pursued to maximise current efforts by ESFRI RIs and build on the technical and thematic knowledge gained in ESFRI Clusters, to deliver new knowledge and new services, and enhanced socio-economic impact. Different levels of integration and connections will continue to build the infrastructure landscape in the Health & Food sector, towards true interdisciplinarity and convergence (see **Figure 5**).

Boundary areas have the potential to provide a new level of integration and organisation. It is proposed that boundary areas can lead to the formation of Interdisciplinary Clusters in order to realize the added value of RIs being connected not only to new RIs but also to other relevant initiatives. Interactions with stakeholders like the healthcare and agri-food sectors and industry will benefit from those formations. This is important in order to continue building the ERA, capitalising on the generated knowledge and translating these into the benefits for society.

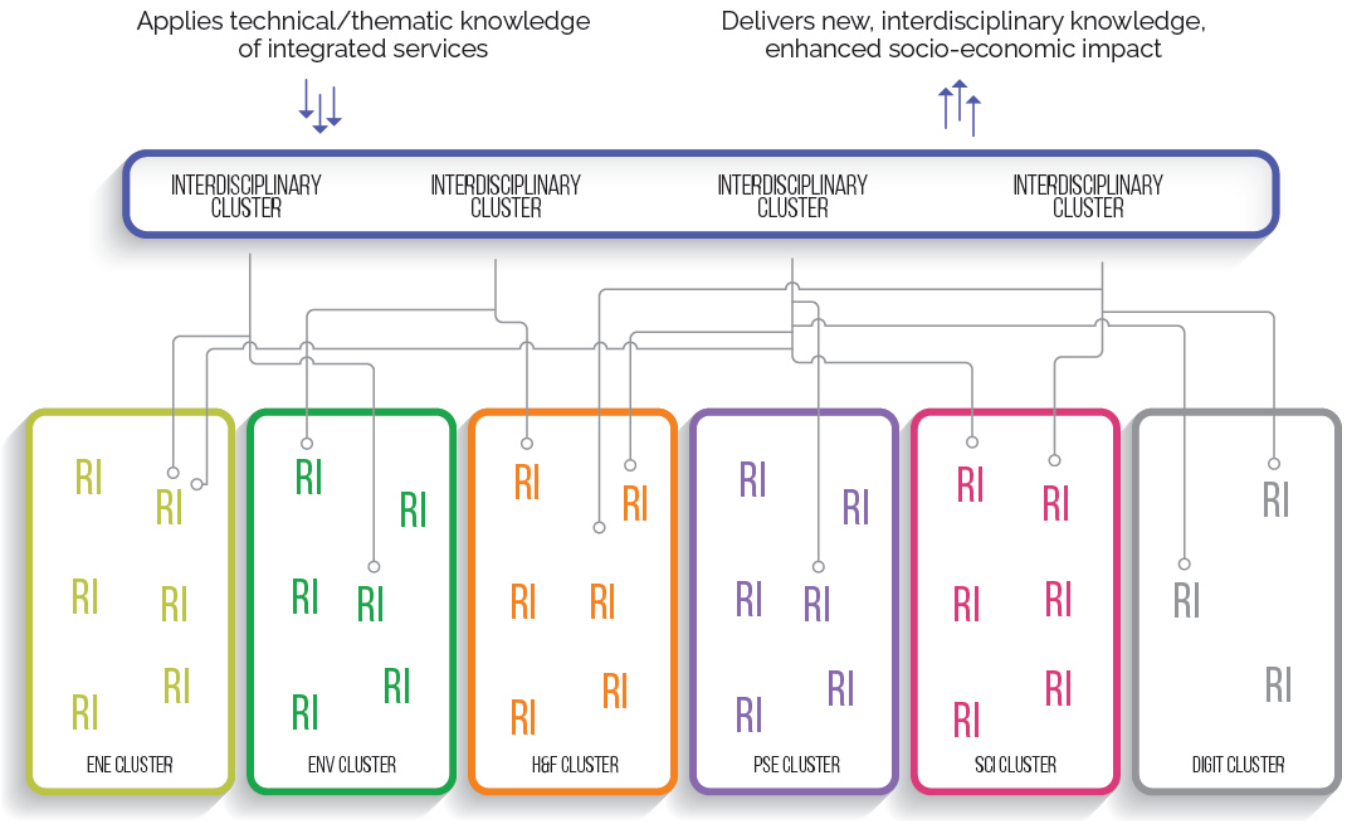

FIGURE 5.
Interdisciplinary clusters - new connections in the ESFRI RIs landscape

GAPS AND CONNECTIONS IN FOOD

In the context of a changing environment, an increasing human population and pressure on land, a concerted effort to continue bringing together national facilities at pan-European level in the field of *animal genetic resources, phenotyping and breeding, animal health* is needed to contribute to address the challenge to produce safe, healthy and sustainable food. Continued RI efforts at EU-level are needed to provide livestock genetic resources, phenotyping and breeding, including large farm animals, poultry and fish; genetic resources for adaptation to climate change and protein production; genomic selection and genetic modification and sustainable intensification for higher feed efficiency, precision livestock farming and precision feeding; platform of technologies and capabilities for epidemiological modelling and surveillance, including host-pathogen interactions and vaccinology towards countering the threats of animal-borne disease. There is a need to proactively combine world-class facilities for the integration, conservation, and coordination of national and international animal genetic stock, and potential stock lines for adaptation to climate change. New efforts should include integrated facilities for bioimaging, digital imaging, genomics, proteomics and metabolomics along with field and veterinary facilities with farm-scale experimental platforms for animal studies and phenotyping, including aquaculture and animal disease facilities, e.g. building on AQUAEXCEL[39], NADIR[40] and VetBioNet[41]. Animal genotype-to-phenotype infrastructures and capability at pan-EU level will have a positive impact on global food production and on European competitiveness, and enhance international effort in this important field.

Food related diseases are costly; the EU national health systems are the most under pressure. The key is to fully understand the interrelation between nutrition and health, particularly the digestive process and the role of food consumption, including the gut microflora, food pathogens, immunology and many other factors, that together can help develop new strategies to deliver healthy and nutritious food and encourage favourable changes in consumption patterns. Regulatory demands relating to health and novel foods impose comprehensive safety assessment procedures and scientific evidence. European research base and expertise in nutrition and food science is unique but it remains highly fragmented and, in some areas and countries, it is below the critical mass[42,43,44].

New infrastructure efforts are needed at EU-level in the field of *food, nutrition and processing*. There is a need to connect RIs across EU and globally, and across the entire food chain. Food systems cover a number of intertwined important areas, spanning social, cultural, economic, geo-political, and environmental dimensions, and involving a great diversity of stakeholders. There is a role for Research Infrastructures to be able to connect food systems and stakeholders. The **ESFRI Projects AnaEE, METROFOOD-RI, EMPHASIS**, and other EU initiatives like the EC-funded project Richfields contribute to achieve this aim, from sustainable food production to consumer behaviour. The **ESFRI Landmark EMBRC ERIC** supports fundamental and applied research activities towards sustainable solutions in the food sector, as well as in health and the environment.

Connections to food and feed production systems are key. The **ESFRI Project EMPHASIS** is central to this stage, currently establishing connections to relevant ESFRI Projects and Landmarks as well as other infrastructures and large scale initiatives. The International Wheat Yield Partnership (IWYP), led by public funders of UK, France, USA, Canada, Australia, India, Mexico is a global mechanism established in 2012 bringing together funding from public and private research organisations from around the world with the goal to raise the genetic yield potential of wheat by 50% in 20 years. This important gap area is of interest to many EU countries and current efforts to connect relevant infrastructures and large scale initiatives should continue[45,46].

The **ESFRI Project METROFOOD-RI** aims at providing high quality metrology services in food and nutrition, comprising an important cross-section of highly inter-disciplinary and inter-connected fields throughout the food value chain, including agro-food, sustainable development, food safety, quality, traceability and authenticity, environmental safety, and human health. This gap area is vast and there are in addition several IA addressing complementary aspects on food and nutrition, which are breaking ground for future infrastructure in nutrition and health, e.g. FoodManufuture EuroFIR, NuGO, Food-4Me, Eurogene, EURRECA, QuaLiFY, and EuroDISH[47,48]. In addition, the combination of fundamental science, translational research and clinical trials, positioned alongside a major clinical gastroenterology service and tissue repository, will ensure a seamless interface between research, clinical practice and the pharmaceutical and biotechnology industries, also cross linking with RIs at the boundary areas.

Food production and its accessibility are increasing worldwide. Legal and ethical issues are critical and have to be addressed as well as information and communication. Nanotechnologies create the possibility of foods with new flavours and textures, and also healthier food products with reduced salt, fat or sugar content or increased vitamin and nutrient content, using nanoencapsulation. Due regard needs to be given to safety and sustainability aspects in their broadest sense as well as to public perception and stakeholder engagement in align-

39. Aquaexcel
http://www.aquaexcel.eu/

40. NADIR - The Network of Animal Disease Infectiology Research Facilities
https://www.nadir-project.eu/

41. VetBionet
http://www.vetbionet.eu/

42. JRC Foresight study, Tomorrow's healthy society – Research priorities for foods and diets, 2014
https://ec.europa.eu/jrc/sites/jrcsh/files/jrc-study-tomorrow-healthly-society.pdf

43. 3rd and 4th SCAR foresight exercises
https://ec.europa.eu/research/scar/pdf/ki-01-15-295-enn.pdf

44. ETP Food for Life Implementation Plan, 2018
http://etp.fooddrinkeurope.eu/

45. The International Wheat Yield Partnership (IWYP)
http://iwyp.org/

46. Wheat Initiative
http://www.wheatinitiative.org/

47. EuroDISH
http://www.eurodish.eu/

48. Precision agriculture and the future of farming in Europe
http://www.europarl.europa.eu/RegData/etudes/STUD/2016/581892/EPRS_STU(2016)581892_EN.pdf

ment with the principles of Responsible Research and Innovation. These principles apply to all Health & Food areas but are flagged here for their relevance in the nanotechnology field.

The increasing digitalisation of agricultural practices is realising the production of plant and animal products with ever higher efficiency and ever lower environmental impact – Precision agriculture and the future of farming in Europe. Precision agriculture is a modern farming management concept using digital techniques to monitor and optimise agricultural production processes. Beyond sustainable food production, precision agriculture offers technologies for producing more food with less input, e.g. sensor-based monitoring systems provide farmers with better information and early warnings on the status of crops, and improved yield forecasts. Precision agriculture also plays a major role in animal husbandry. The **ESFRI Projects EMPHASIS** and **AnaEE** aim to collaborate in bringing innovative solutions for a sustainable intensification of agriculture. By integrating the study of plant phenomics and agricultural ecology they hope to foster the development of novel scientific concepts, sensors and integrated models[49]. Integrated approaches including e-infrastructures are needed to systematically predict, diagnose, prevent and treat plant and animal disease, and to device effective responses to mitigate the impact on agri-ecosystems. Legal and ethical issues are critical as well as information and communication.

Health & Food RIs and their connections with ENV SWG and ENE SWG RIs are critical to address issues associated with *agriculture and land-use change*, food and non-food systems, and bioenergy. The **ESFRI Project AnaEE** is working with the **ESFRI Landmarks ICOS ERIC** (Integrated Carbon Observation System, ENV), **LifeWatch ERIC** (e-Infrastructure for Biodiversity and Ecosystem Research, ENV), and others in the EC projects ENVRI and ENVRI+, Common Operations of Environmental RIs linking across e-infrastructure initiatives. The links to the social sciences are also important. The global demand for food includes challenges regarding efficiency, resilience and sustainability. The field of bioenergy and biorenewables in particular links to energy and environmental facilities.

The sustainable production and conversion of biological raw materials for use as sources of renewable energy, materials and chemicals can provide alternatives for diminishing fossil resources and drive the growth of the knowledge based bio-economy. Addressing the demand for sustainable supplies of materials, fuels and food through biological means required the use of biological resources towards environmental and economic sustainability. An effort at European level is required to bring together pilot-scale facilities, demonstrators and up-scaling facilities to enable access to the production and processing of materials, chemicals (e.g. antibiotics) and energy, using biological resources, including plant, algae, marine life, fungi and micro-organisms. The **ESFRI Project EU-IBISBA** proposes a distributed RI on industrial biotechnology with applications in energy (liquid biofuels), chemicals (organic acids), materials (bioplastics) and ingredients for the food, feed, cosmetics and pharma sectors (enzymes, antioxidants, antibiotics). The **ESFRI Project EU-IBISBA** aims to deliver translational research in industrial biotech, allowing researchers to access cutting-edge technology, infrastructure and expertise to move projects up to TRL6. The **ESFRI Project EU-IBISBA** has the potential to accelerate TRL2 to TRL6 processes, and in reducing time to market. It will interact with and connect to existing infrastructures such as the **ESFRI Projects ISBE** and **MIRRI**, the **ESFRI Landmarks BBMRI ERIC**, **ELIXIR**, **INSTRUCT ERIC**, and **EU-OPENSCREEN ERIC**, and other RIs in the environment, and energy sectors. The infrastructure uses synthetic biology as one of their approaches. Synthetic biology applies engineering to the biosciences, seeking to design and construct/modify new or existing biological parts and systems to deliver novel functions that do not exist in nature. The field is expected to impact many sectors of the economy, and to provide tools to better tackle areas of great social and environmental interest, including health, energy and food security[50]. Synthetic biology is both highly interdisciplinary and technically and scientifically demanding. It and also addresses a range of social, economic, ethical, and legal issues.

GAPS AND CONNECTIONS IN HEALTH

The future of health research offers high potential to patients, to citizens, and the economy. The move in the sector towards precision and stratified medicines and personalised healthcare at much lower cost to the consumer brings with it a need to test new technologies and provide multi-scale facilities as test-beds for pharmaceutical and biopharmaceutical (therapeutics) manufacturing. These activities apply primarily to industries for technological development based on academic input and evidence. Investment to date has focused more on fundamental science and discovery, meaning that there is a gap between discovery and actual manufacture. This area should constitute an excellent platform of technology development and include the complete manufacturing process from a scientific, engineering, regulatory and supply chain perspective, with the ultimate aim of providing affordable access to innovative therapies in collaboration with the **ESFRI Landmarks EATRIS ERIC**, **ECRIN ERIC**, and **EU-OPENSCREEN ERIC** and other relevant RIs, and Innovative Medicines Initiative (IMI2). Research in this area is expected to be highly innovative and will lead to three key benefits: better diagnosis and earlier interventions, more efficient drug development, and more effective therapies. Existing infrastructures such as the **ESFRI Landmarks BBMRI ERIC**, **EATRIS ERIC**, **ECRIN ERIC**, **ELIXIR**, **ERINHA** and others could connect aiming at providing a full pipeline for drug development.

Advances in the sector of personalised health care require computational approaches, and integration with innovations in biomedical engineering, analytical research, and other relevant fields as well as with social, ethical and regulatory aspects. The challenge of *antimicrobial resistance* and pandemics also calls for an integrated effort. Next generation sequencing technologies and mass spectrometry platforms for genomic, transcriptomic, proteomic, metabolomics and metagenomics applications, coupled with advanced imaging, set the basis for personalised and stratified drug discovery and development. Combined high-end technology platforms with specialised expertise, bringing together hospitals, research centres and

49. European infrastructures for sustainable agriculture. Roy et al. (2017) https://www.nature.com/articles/s41477-017-0027-3

50. ERA-Net SynBio https://www.erasynbio.eu/

the private sector in an integrated network that will offer a point of single access for the development of next generation medicines. All ESFRI Health & Food Landmarks and Projects with applications in health have the capacity to play a significant role in enabling research activities towards developing tailored healthcare interventions and robust models for prevention and treatment strategies, bridging the gap between genomic information and clinical practice.

New therapies are needed in order to cure and treat *complex diseases*. Challenges exist in the development of new applications and new modes of treatment approaches in *imaging, diagnostics and novel therapeutics*. The **ESFRI Landmarks INSTRUCT ERIC**, **Euro-BioImaging**, **INFRAFRONTIER**, **EATRIS ERIC** and **ECRIN ERIC** are of relevance. Interdisciplinary interactions will be critical in order to handle upcoming issues and implications – e.g. in the *ageing population* and neuroscience research[51]. Links of relevance are the Joint Programming Initiative "More Years, Better Lives – The Potential and Challenges of Demographic Change" seeking to map data sources on ageing at the European and national levels[52] and the Knowledge and Innovation Community initiative EIT Health, promoting innovation in healthy living and active ageing[53]. New advances in technologies, such as nanotechnologies, are having impacts on therapeutics, diagnostics, imaging and regenerative medicine, particularly in cardiovascular diseases, diabetes and cancer. Due regard needs to be given to public perception and stakeholder engagement and the principles of Responsible Research and Innovation. Tools for health planning are required. A Health information System is supported by the EC DG SANTE as a joint action to harmonise health indicators and surveillance tools across Europe, and to host health-related databases including population based and clinical registries for diseases, biobanks, health protocols as well as metadata for health determinants.

Longitudinal population studies and cohorts are an invaluable resource for research, in health and disease conditions. These studies gather data over a long period of time and provide a rich resource with connections to several domains. In particular, this is an area to explore together with the ESFRI Social & Cultural Innovation SWG and its Research Infrastructures, which flagged "integration of biosocial data and resources – longitudinal and cohort studies" in their landscape as an important area of connection to Health & Food Research Infrastructures. There is a need to enable a Research Infrastructure environment that will facilitate research on the *human health and wellbeing* at all stages in development, including ageing, nutrition and behavioural studies, and their connections to the social sciences and humanities. There are also geographic, economic and environmental drivers affecting human health and wellbeing. Climate change, extreme weather, dramatic changes in ecosystem services, *environmental pollution and exposure to harmful chemicals* represent a new combination of issues that require an integrated approach at pan-European level. At the heart of this approach is the exposome, taking a holistic view throughout the human lifetime on the effect of exposures to diet, lifestyle, and the environment on human health and disease. The exposome coupled with advanced genetic and medical approaches represents an opportunity to tackle this complex issue by connecting to the landscape of Health & Food RIs and other domains. Ongoing EU projects and networks on human biomonitoring (HBM4EU and EMEP) are important steps to bring together relevant parties[54].

Health & Food RIs provide a framework for applications in other domains, such as anthropological studies, using biobanking, omics, and metabolomics. Cohorts include biological material of specific diagnoses and general populations either longitudinal or case by case. Multidisciplinary databases contain data of different aspects related to the addressed hypothesis. The combination of these has the potential to enable better understanding of disease and the identification of disease mechanisms.

VISION AND PERSPECTIVES

ESFRI has been instrumental and influential in the co-ordination of national decision-making and investment in European RIs in Health & Food. The landscape continues to evolve and it is important to ensure its ability and agility to respond to current and future demands. Significant innovations and new developments often occur at the boundaries of research areas. To continue cementing the critical role of distributed RIs in Health & Food as they progress in their lifecycle, it will also be important to connect infrastructure efforts with other domains. This is territory largely unexplored and where Health & Food RIs have the potential to pioneer new ways of working and realise true interdisciplinarity.

There is a need to develop well-established procedures for the systematic assessment of the social and economic impact of Health & Food RIs, to demonstrate effective use of resources and accountability for public money, to inform future decision making and evidence for policy-making, to demonstrate evidence of societal and economic benefits and to ensure their long term sustainability. Overall, this will help demonstrate the collective impact that the distributed RIs in Health & Food have had in shaping the landscape of research infrastructures in the last 12 years since the first ESFRI Roadmap was published, and will signal their potential to transform the landscape in the years to come.

51. The 2015 Ageing Report
http://ec.europa.eu/economy_finance/publications/european_economy/2015/pdf/ee3_en.pdf

52. The Data Mapping Project
http://www.jpi-dataproject.eu/

53. EIT Health
https://www.eithealth.eu/about

54. Towards Cleaner Air Scientific Assessment Report 2016
http://www.unece.org/index.php?id=42861