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## 2021 IBISBA report: current status

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# 2021 IBISBA Report

Current Status



**IBISBA**

SHARING  
THE WAY  
TO INNOVATION

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<b>04</b>	<b>Industrial Biotechnology Innovation and Synthetic Biology Accelerator</b> 04 - Sharing the Way to Innovation
<b>05</b>	<b>Executive Summary</b>
<b>07</b>	<b>Stating the Case for a European Research Infrastructure to Support Biotechnology</b> 07 - Driving the Circular Bioeconomy 07 - Delivering Europe's Green Deal's 09 - Biotechnology as a Vital Component of the Green Deal
<b>11</b>	<b>Building Tomorrow's Biotechnology</b> 11 - Key Scientific and Technology Challenges 12 - Scientific Challenges 12 - New Knowledge for Bioengineering and Biomanufacturing
<b>14</b>	<b>The Status of Biotechnology Infrastructure in Europe and Beyond</b> 15 - International Dynamics of Industrial Biotechnology and Research Infrastructure Business Models 17 - Funding Schemes and Business Models
<b>21</b>	<b>IBISBA, a Unique Distributed European Research Infrastructure for Biotechnology</b> 21 - IBISBA's Strategy 22 - IBISBA's Value Proposition
<b>25</b>	<b>Achievements and Status of IBISBA</b> 25 - IBISBA is Present in 9 European Countries 26 - Defining IBISBA's Uniqueness Among European Life Science Research Infrastructure 34 - Achievements and Progress Towards Implementation of IBISBA 35 - Training and Expertise 36 - Defining the Business Framework for Success IBISBA's Governance Structure
<b>44</b>	<b>Towards ERIC-IBISBA - Next Steps</b> 44 - Timeline of the Preparatory Phase
<b>46</b>	<b>Towards ERIC-IBISBA - 1st Steering Committee Meeting</b> 46 - Remote Meeting of IBISBA Steering Committee 47 - Country-Specific Statements

# Industrial Biotechnology Innovation and Synthetic Biology Accelerator

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## Sharing the Way to Innovation

Our motto “sharing the way to innovation” encapsulates several ideas that underpin IBISBA. Through sharing, we believe that biotechnology will gain from greater integration of scientific research and the research infrastructures that support it. The co-development of research strategies and methods designed to address outstanding challenges in biotechnology will speed up R&D projects and diminish wasteful duplication of research efforts. Sharing also implies irrigating the whole R&D process with relevant knowledge. This requires digital tools to create a knowledge commons and mutualised business practices to create shared interfaces between infrastructures services.

The notion of a ‘way’ evokes a pathway and a dynamic process that leads from a beginning to a conclusion. The beginning for IBISBA is the wealth of knowledge and concepts that emerge from our fundamental and applied research. To reach industry readiness and thus the conclusion, these assets need to be translated into prototypes and pilot-tested processes, building in fitness for industrial deployment. This is a translational **research process that bridges the gap between academic research and industrially competitive R&I**. Logically, the inclusion of ‘innovation’ is also vital to understand IBISBA’s activities and position as an infrastructure.

IBISBA **aims to stimulate innovation**, working with academic and industry-based researchers to devise technical solutions that will help to attain a range of UN sustainability goals.



# EXECUTIVE SUMMARY

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The mission of IBISBA is to provide a world-class infrastructure **enabling cutting-edge research** and supporting the development of biotechnology towards a circular economy. To achieve this, IBISBA draws together within an interoperable network some of Europe's most significant, public-operated research infrastructure, endowing them with unprecedented ability to **collectively operate modular service workflows**, seamlessly linking services produced by individual facilities to support whole R&D project life cycles.

The target business model for IBISBA primarily addresses **impact in biotechnology, focusing scientific excellence on the innovation gap** that separates fundamental research from industrial innovation. In this regard, IBISBA aims to be an infrastructure for a **mixed user community**, being attractive for both academics and private industry researchers. To succeed, IBISBA will address the key causes of failure in transversing the gap in biotechnology, drawing on the **diverse multidisciplinary expertise** held by its participant facilities and present in its user community. Moreover, IBISBA will promote strong pan-European synergies in the field of biotechnology, ensuring that Europe remains at the forefront of innovation in the sector, while optimizing public investment in the area.

To date IBISBA's proponents have made good progress towards the creation of a world-class infrastructure, **building FAIR compliant digital tools**, performing network reinforcement activities, outreach to other European research infrastructures and **R&D aimed at establishing best practice and standards**. Moreover, IBISBA has demonstrated its ability to **open access**, promote **transnational researcher mobility**, and **disseminate collective knowledge** in the form of training and expertise for public stakeholders. Finally, in a major step towards the implementation of a permanent research infrastructure, **IBISBA was added to the ESFRI strategic roadmap in 2018**, thus conferring its proponents with the responsibility to further advance the ambition towards realisation.

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In 2020, IBISBA partners launched a preparatory phase. This 4-year long process aims to further define IBISBA's business model, identify the most suitable legal model and devise a governance structure and financial plan for implementation and operation. Eighteen months in from the beginning, the preparatory phase has now delivered its first conclusions. The future IBISBA legal entity will service national nodes, composed of research facilities owned by public entities (RTOs, universities), using a central component that will provide overarching management and coordination. Considering IBISBA's ambitions and the desires of its stakeholders, the preferred legal structure to deliver IBISBA is a **European Research Infrastructure Consortium (ERIC)**, although an 'Association Internationale Sans But Lucratif' (AISBL) partially responds to IBISBA's needs and stakeholder expectations.

In summary, initial work performed since late 2017 supports the feasibility of IBISBA and reveals how this research infrastructure can **drive new scientific discovery and innovation** in the field of biotechnology and **support European R&D and industrial leadership in the area**. To achieve the next steps in IBISBA's preparatory phase, founding Member Countries are being asked to provide a mandate to IBISBA's stakeholders, encouraging them to move forward and prepare the **creation of a legal entity as the vehicle of IBISBA's ambitions**. It is expected that the second semester 2021 will provide the opportunity to further consolidate the business model and build a viable business plan to implement IBISBA as a legal entity in the second semester 2023.

## Glossary

**Biofoundry:** highly automated facility that performs molecular biology related operations using high-throughput robotic liquid-handling and analytical equipment. Biofoundries are designed to accelerate bioengineering operations using, among others, the engineering design-build-test-learn conceptual framework, workflows and advanced software.

**Biocatalyst:** a catalyst of biological origin that accelerates chemical reactions. Nucleic acids, enzymes, microorganisms, and entire microbial ecosystems are biocatalysts.

**Biotechnology:** the use of biocatalysts to drive processes that deliver societally relevant products and services. Industrial biotechnology focuses on the application of biotechnology to manufacturing industries. Industrial biotechnology is applied to make antibiotics, medicines, most amino acids, flavours, biofuels, and biobased chemicals. Environmental biotechnology focuses on processes that provide services such as wastewater treatment, depollution and remediation, environmental monitoring, and waste upgrading and agriculture.

**Bioengineering:** a discipline that applies engineering principles of design and analysis to biological systems. An underlying postulate in bioengineering is that biological systems can be modified to deliver specific functions. Synthetic biology is the most advanced form of bioengineering. It uses, among other methods, DNA manipulation, a high degree of automation and digital technologies to not only modify biological systems, but also to create new ones.

**DBTL:** the bioengineering Design-Build-Test-Learn cycle. This conceptual framework is widely used in synthetic biology.

# Stating the Case for a European Research Infrastructure to Support Biotechnology

## Driving the Circular Bioeconomy

The European Union pioneered the concept of a knowledge-based bioeconomy and is a strong advocate of the circular bioeconomy. This is because it is well-recognised that the circular bioeconomy is a vital component for Europe's future well-being and economic sustainability. This is reflected in several policy strategies such as the Green Deal, European Bioeconomy strategy and Smart Specialisation. Adoption of the circular bioeconomy will provide Europe with the means to reduce its dependence on fossil resources and gain in autonomy in many market sectors. Moreover, it is anticipated that this economic concept will stimulate industrial renewal and diversification, providing new employment and economic growth to the Continent's communities, whilst increasing environmental sustainability.

## Delivering Europe's Green Deal

The Green Deal is an ambitious policy launched by the European Commission to ensure that Europe's post-pandemic economy will be modern, resource-efficient, and competitive. To attain this, the overarching aims of the Green Deal are to deliver zero greenhouse gas (GHG) emissions in 2050, decouple economic growth from resource use and create an inclusive economy.





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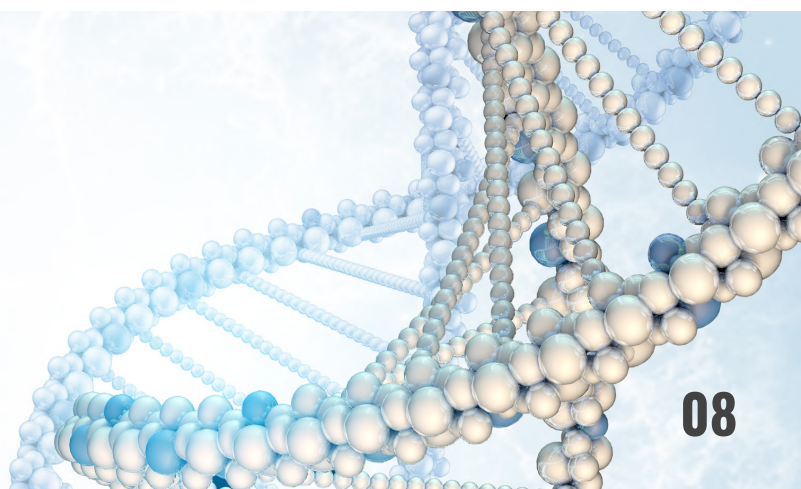
An intrinsic component of the Green Deal's success will be a circular bioeconomy that uses biobased resources to provide clean energy, carbon neutral products and a variety of environmental services that contribute to maintain soil fertility, reducing atmospheric pollution, and enhancing biodiversity. To reach these goals a range of new technologies is required. These will provide the basis for modernised, clean industrial processes, clean, affordable, and secure energy, new sustainable building materials, a cleaner, healthier environment, and a more sustainable agri-food industry.

**Biotechnology is prominent among the technologies that will be essential to deliver the Green Deal.**

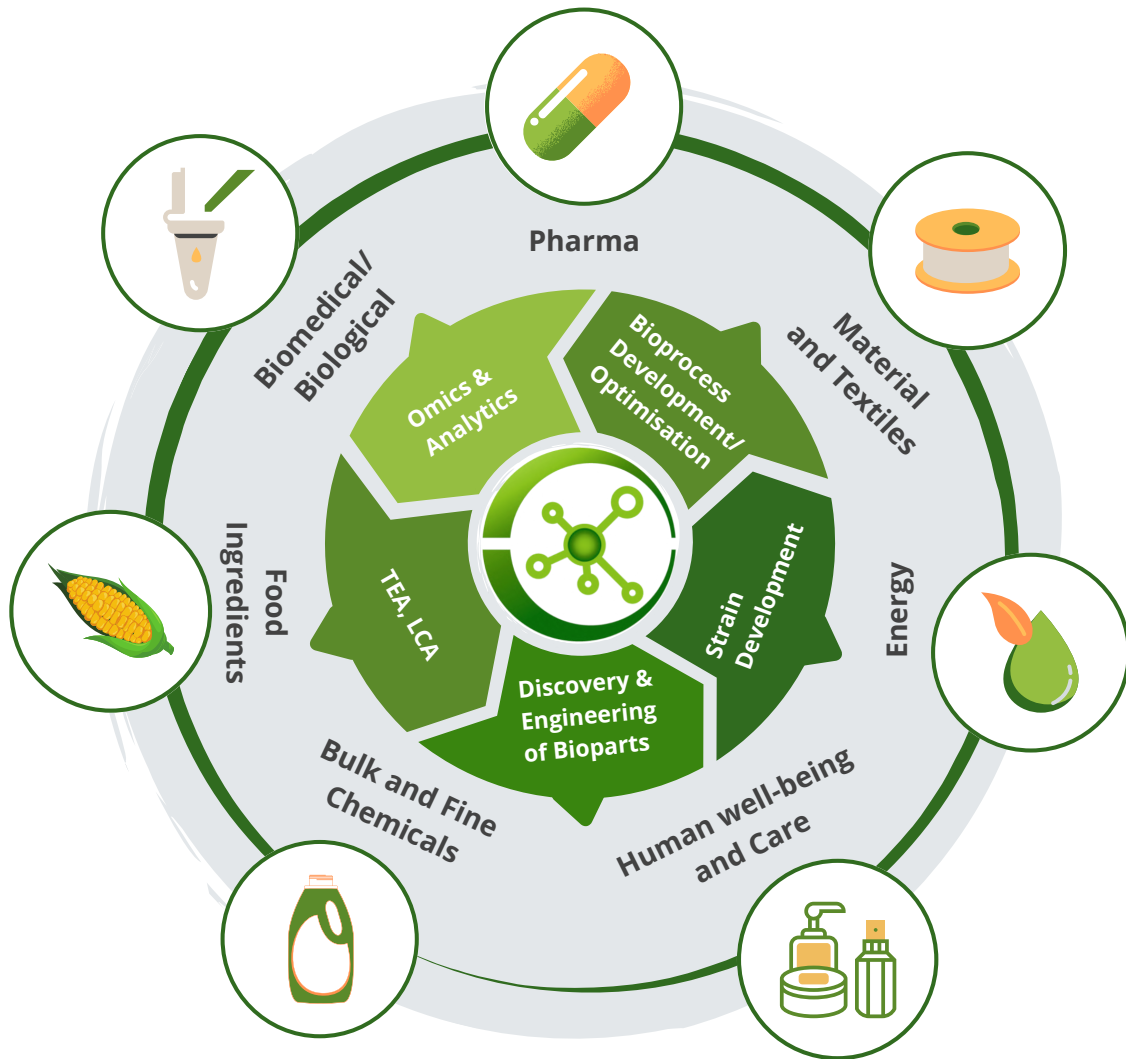
### What is Biotechnology and How Can it Deliver Sustainable Processes, Products, and Services?

Biotechnology uses living organisms and their components (e.g. enzymes and nucleic acids) to convert raw material into products and related services. Advantageously, living organisms are exquisitely adapted for the conversion of biobased resources, and their catalytic functions are both extensive and amenable to bioengineering. Consequently, biotechnology is identified as a key enabling technology for the circular bioeconomy, because it empowers the development of (i) alternative, cost-effective manufacturing processes to produce existing products, (ii) access routes to myriads of novel products and services (e.g. biogas production and recycled fossil-based materials) and (iii) cleaner manufacturing solutions, compliant with increasingly stringent environmental regulation and changing societal values. In this respect, biotechnology is ideally positioned to contribute to the circular bioeconomy transition and fulfil the ambitions of Europe's Green Deal and many UN Sustainable Development Goals. For these reasons, **Europe has put forward biotechnology as a central pillar of innovation and identified it as an advanced technology for industry.** Indeed, it is expected that biotechnology's role in the circular bioeconomy will be analogous to that of chemistry in the petroconomy.

As Nature's catalysts, enzymes are fundamental to biotechnology. These extraordinary biocatalysts support the functioning of all living systems and display amazing aptitude to catalyse an astonishingly large number of chemical reactions. In living organisms, enzymes usually work together in an ordered fashion to perform complex cascade reactions that characterise metabolic processes. These processes provide the basis for the synthesis of an almost infinite array of organic compounds that are suitable for a wide variety of market products, including biofuels, bulk and fine chemicals, ingredients for food and feed, cosmetics, medicines, and pharmaceuticals, among others (Figure 1).



Moreover, enzymes and living organisms can be harnessed to provide services such as wastewater treatment, CO<sub>2</sub> capture, environmental remediation, crop protection etc. Exploiting individual enzymes and the power of living organisms to provide such products and services is the business of biotechnology.



**Figure 1.** IBISBA services are relevant to a wide array of market sectors covered by biotechnology.

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## Biotechnology as a Vital Component of the Green Deal

Biotechnology is a so-called 'cleantech' because bioprocesses generally operate in moderate conditions of temperature and pH and mostly eliminate the need for hazardous chemicals and solvents. This implies that biotechnology is well-positioned to renovate European manufacturing industries, conferring them with a lower environmental footprint and thus providing a route towards a clean, circular economy. However, the benefits of biotechnology extend beyond environmental sustainability. This technology family provides the means to tackle strategic issues, such as manufacturing autonomy and social inclusiveness. Many of the raw materials used in biotechnology-based industries are sourced locally, meaning that it is possible to develop territorially-anchored value chains that provide local jobs and provide, for example a secure, domestic supply of energy. Moreover, the market reach of biotechnology is extensive, spanning environmental services to industrial products, including a range of sustainable materials for packaging and construction. At industry level, the circular bioeconomy will be coupled to a profound modernisation of manufacturing processes, which will increasingly rely on key enabling technologies such as biotechnology, automation, and digital solutions. Furthermore, it is anticipated that the circular bioeconomy will create new, multifunctional value chains that will not only deliver goods, but also services to society and the environment. Advantageously, the versatility of biotechnology means that more sustainable materials can be both manufactured and recycled using processes driven by enzymes or microorganisms.



While the potential of biotechnology is enormous and remains to be fully exploited, biotechnology is already a reality in the European economy. According to EuropaBio, in 2018 biotechnology contributed €34.5 billion gross value added (GVA) and was directly responsible for 230,000 jobs, meaning that the sector is already a key one in Europe's economy [1]. Furthermore, most analysts agree that growth of biotechnology will continue to progress in the coming years. In 2030, it is expected that employment in the biotechnology value chain will increase to more than one million jobs, contributing up to €100 billion to the EU economy. As the need for solutions to global challenges becomes increasingly urgent, the need to prioritise and invest in innovative solutions provided by cutting-edge technologies becomes imperative, as does the need to stimulate market uptake of bio-based products.

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[1] Haaf et al (2020) Measuring the economic footprint of the biotechnology industry Europe (prepared for EuropaBio).

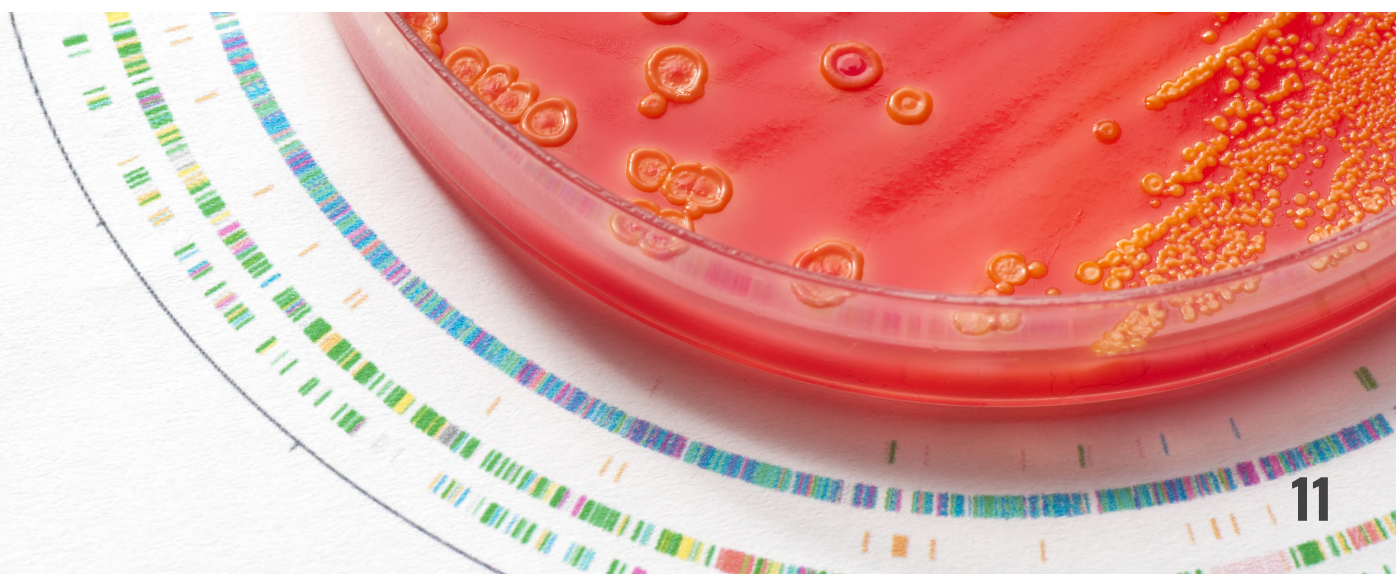
# Building Tomorrow's Biotechnology

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## Key Scientific and Technology Challenges

In recent decades, biotechnology has advanced by leaps and bounds. Strong progress in systems biology, advances in DNA sequencing and synthesis, genome engineering (e.g. CRISPR Cas9 technology), mRNA technologies (e.g. COVID-19 vaccines), cell- and ecosystem-scale, omic-based analytics and so forth have paved the way for vast improvements in the field of bioengineering. Synthetic biology is an emblematic development that is revolutionising the way biocatalysts are designed and built, providing the bioengineer with new methods and tools to design robust enzymes and microbial systems that form the basis for new, more sustainable biomanufacturing processes and biobased services.

Despite the great promise and a large corpus of evidence that demonstrates the power of biotechnology, the biobased manufacturing industry is still in its infancy and requires ongoing research and development to bring it to maturity and promote its uptake by the commercial sector. In the context of a circular bioeconomy, this is vital because this economic paradigm must evolve within a commercial framework dominated by fossil-based processes and products and underpinned by an extremely mature, efficient industrial (petro)chemistry sector.



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## Scientific Challenges

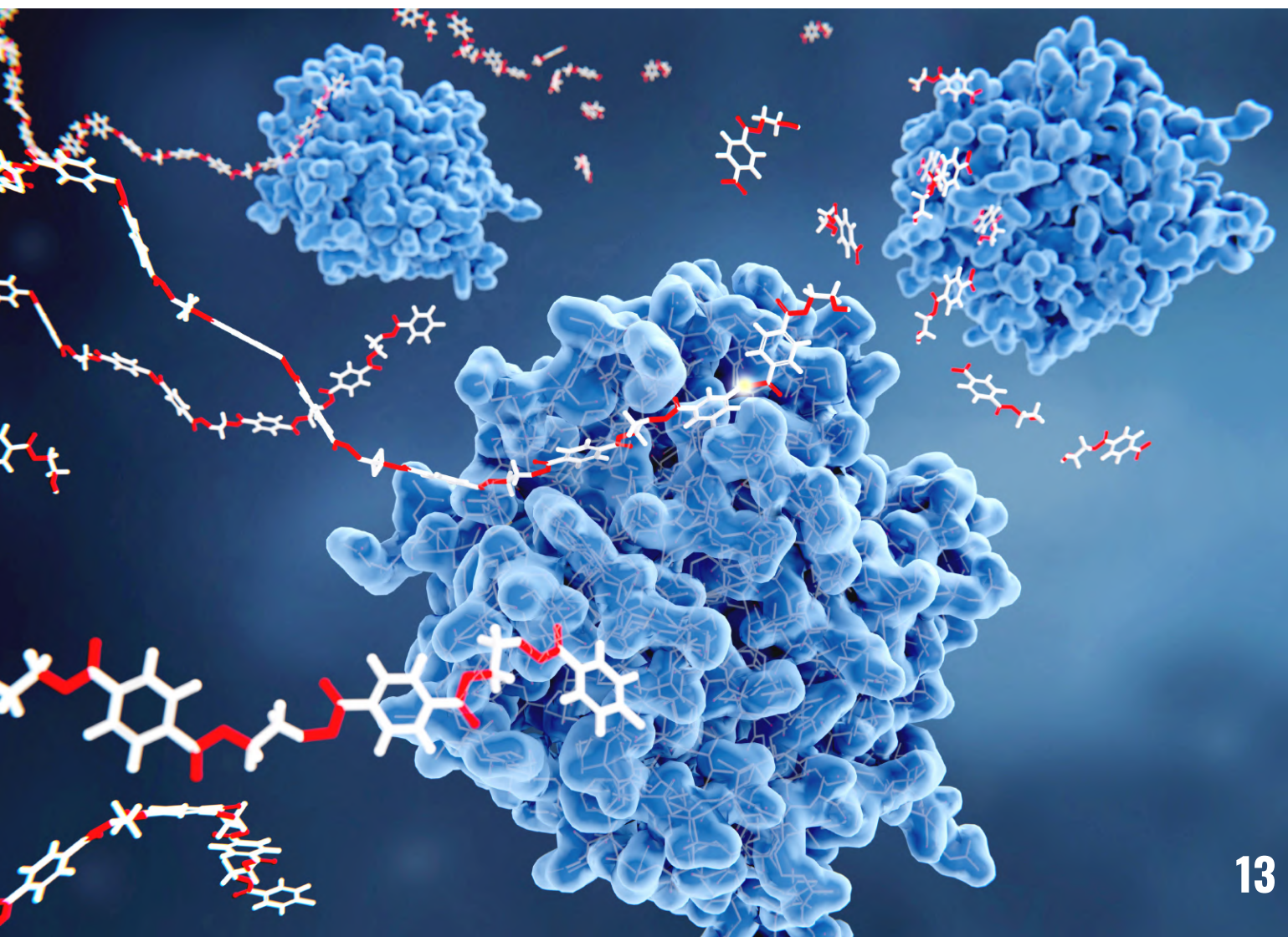
As the current pandemic attests, biological processes are inherently complex due to the many layers of interactions among myriads of components, even those within relatively simple biological systems. Biological processes are thus often more difficult to understand, predict and steer, than most chemical processes. This has held back the development of biotechnologies, in particular when physical or chemical processes for equivalent purposes are available, efficient and economically viable. Furthermore, in contrast to industrial chemistry, research in biotechnology often fails to scale. This is logical, because process developers in biotechnology do not have the extensive expertise of chemical engineers who rely on almost two hundred years of experience that has provided the current industrial maturity. Scaling up problems in biotechnology are related to multiple factors and many are often linked to the current lack of sufficient understanding of physical and biological phenomena. However, others are related to a historical division of labour between biosciences and chemical engineering.

## New Knowledge for Bioengineering and Biomanufacturing

Science and technology challenges in biotechnology and in the scale-up process are numerous. However, among these it is relevant to mention the need for:

- **better understanding** of regulatory processes and (dynamic) interactions in biological systems. To meet this challenge more detailed multiscale models describing cell (or ecosystem) regulatory and interaction networks are required. This in turn calls for more knowledge about the mechanisms that underpin the different parts of regulatory networks. Moreover, it is necessary to deepen knowledge on network dynamics in a bioreactor environment where the cell or microbial ecosystem is under operating constraints. New models should provide digital twins to guide bioengineering, building in design features such as greater stability to stress factors, including oxygen starvation, nutrient gradients, contamination or fluctuations in operating conditions.
- **better knowledge** of the phenotype-genotype relationships of the biocatalysts underpinning the envisaged processes. This requires substantially more insights into the functions encoded by genetic traits in microbes and microbiomes, for instance through systematic, high-throughput functional analysis. In combination with the use of semantic and artificial intelligence technologies, this should provide ways to identify industrially relevant traits in microbiomes and metagenomes (e.g. for tolerance to solvents, chemicals or process conditions). In turn, this provides the means to transfer traits into microbial chassis, compatible with the process under development.

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- **better translation** of large-scale conditions into designs and into small scale testing (scaling-down). Scaled-up processes are characterised by a series of physical phenomena that are unimportant at small scale. These include mixing effects (e.g. turbulence and heterogeneity), heat transfer, hydrostatic pressure etc. It is extremely difficult to simulate these phenomena at a small scale, but it is vital to predict their effects to improve early lab-scale prototypes. Moreover, achieving economic viability at the large scale involves significant compromises regarding a range of parameters including raw material purity, use of chemicals (e.g. to control pH), and water reuse. Understanding the importance of these parameters on process performance and on biological processes will be important to capture these constraints in the form of design features in biocatalysts.
  - **better integration** of commercial-scale knowledge into biocatalyst and bioprocess designs. Ideally, the design of bioprocesses should begin at the end (i.e. the product or service in a competitive market environment) driving knowledge relating to economic, environmental, and social contexts in backwards along the innovation pipeline, integrating this knowledge into concepts and prototypes. To achieve this, ex ante multi-criteria analysis and optimisation systems are required. In turn, this calls for an acceleration in the development of models for the different unit operations that characterise bioprocesses.



# The Status of Biotechnology Infrastructure in Europe and Beyond

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Historically, Europe has played a leading role in the development of research in biology and was an early player in biotechnology, being the birthplace of several world-leading biotechnology-based companies. Today, the EU is well-endowed with human talent and research infrastructures (RI) required to further develop biobased manufacturing.

The vast majority of biotechnology-focused RI in Europe is nationally or regionally based and is rarely organised to provide cross-border access, although networking initiatives such as Pilots4U [2] promote transnational access to pilot-scale facilities. However, more than networking, **translational research requires strong integration of research and technology services**, a challenge that has so far been poorly addressed in the biotechnology landscape, although some more integrated national research infrastructures are in operation. Examples of geolocalised integrated infrastructures are the Industrial Biotechnology Innovation Centre (IBioIC) located in Glasgow (Scotland), the Austrian Centre for Industrial Biotechnology (ACIB) and Toulouse White Biotechnology (TWB) located in Toulouse (France), while others are embedded operations in larger research and technology organisations such as VTT in Finland.

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[2] [www.biopilots4u.eu](http://www.biopilots4u.eu)



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## International Dynamics of Industrial Biotechnology and Research Infrastructure Business Models

**Landscape analysis** of biotechnology and synthetic biology infrastructures reveals a wide variety of organisations whose features differ in terms of location, technological expertise, services, sectorial positioning, customer profile and overall mission.

**Analyzing investment and dynamics** at a state level reveals that the United Kingdom (UK) has led investment in biotechnology for many years, creating an attractive space for external company investors. Currently, the UK stands out as the European country that boasts the largest number of biotechnology companies, with Germany and France respectively being positioned in second and third positions. In terms of infrastructure, UK public investment has focused on accelerating the development of synthetic biology, with the creation of six multidisciplinary Synthetic Biology Research Centers and DNA synthesis capacity. The upscaling relay for research performed in these centres is provided by other innovation facilities, for example IBioIC in Glasgow and the National Industrial Biotechnology Facility in Wilton (Centre for Process Innovation (CPI)). In Germany, a notable example of infrastructure investment in the field of biotechnology is the centre for Chemical-Biotechnological Processes (CBP, Leuna), which forms part of the larger Fraunhofer Institute for Interfacial Engineering and Biotechnology (IGB). In the Netherlands, the Bioprocess Pilot Facility in Delft and AlgaeParc in Wageningen (focused on light-driven processes) provide state-of-the-art facilities enabling companies and knowledge institutions to develop new sustainable production processes. Finally, among the vital elements in France's biotechnology innovation landscape are TWB, a product of a central government call for preindustrial demonstration facilities, PIVERT (Picardie Innovations Végétales Enseignement et Recherches Technologiques), an innovation facility focused on biobased chemistry and GENOPOLE, a biocluster focusing on genomics-driven R&D for cutting-edge projects in biotechnology. Obviously, other examples of biotechnology-focused infrastructures exist in many other European members states, especially when the analysis is extended to the regional level. Globally speaking, **the coordination of biotechnology-focused infrastructures at the European level is lacking** and even national coordination is rarely a strong feature of the landscape. When coordination does exist, it is often at a local level in the form of clusters and business parks (e.g. DTU Biosustain, which is part of a dense biotech ecosystem that encompasses Copenhagen and Malmö). Overall, this leads to a rather **fragmented innovation landscape**.





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## Biotechnology in Asia

Beyond Europe, Asia is a zone of rapid economic growth that is generating exciting possibilities and significant efforts in terms of research, particularly in biotechnology. Logically, investment has also focused on research infrastructure, especially in countries such as Singapore, Japan, South Korea, and China. Like in most countries, the bridgehead for the development of biotechnology is the biopharmaceuticals sector. To develop these activities, China is focusing on the development of clusters, especially in the Beijing-Tianjin-Hebei area (northeastern China), the Yangtze River Delta (Shanghai area) and the Pearl River Delta, focused on Guangzhou and Shenzhen [3]. These clusters are composed of different industry stakeholders, including research infrastructures (e.g. Guangzhou Bioprocess Academy), but it appears that a smooth continuum between academic research and business innovation has yet to be achieved [4]. Elsewhere in Asia, single-site infrastructures, such as A\*STAR Biotransformation Innovation Platform (BioTrans, Singapore), tightly linked to academia are observed.

## Biotechnology in the USA

Unlike Asia, biotechnology in the USA is not recent and its positive dynamics are longstanding and well-founded. The American biotechnology landscape is characterized by excellent science and research infrastructures well connected to a very dynamic business sector, with a high level of porosity characterizing the different components of the ecosystem. Building on such strong foundations and its traditional approach of building state-based clusters (e.g. the bay area in California), the USA is also innovating by exploring the benefits of cross-state distributed research infrastructure; the Department of Energy implemented four Bioenergy Research Centres 15 years ago and more recently funded the Agile Biofoundry, while the recently created BIOMADE USA [5] distributed initiative has been launched using a combination of Department of Defense funding and private financing.

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[3] Moore, S. (2020) China's role in the global biotechnology sector and implications for U.S. policy. Washington, D.C. Brookings Institution; 2020.

[4] Huggett, B. 'Innovation' nation. *Nat Biotechnol* 37, 1264–1276 (2019). <https://doi.org/10.1038/s41587-019-0306-9>

[5]<https://www.manufacturingusa.com/institutes/biomade>

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## Funding Schemes and Business Models

### Public-Private Partnerships

Research infrastructure operating in the **translational research space must be organised to mobilise and align intellectual resources** held by different stakeholder groups. This involves bringing together a variety of specialists representing different academic disciplines and industry sector professions (e.g. industrial R&D, industrial process engineers, product managers etc.). This is vital to accelerate innovation, avoiding or attenuating the effect of pitfalls encountered when a research-inspired concept is faced with applicative reality. In practice, this type of multi-stakeholder organization is exemplified by public-private partnerships (PPPs), commonly found in the biotechnology environment. In both Europe and the USA this kind of organization is supporting research infrastructure initiatives such as IBioIC, TWB, BPF and BIOMADE USA and also joint programming initiatives such as the recently announced Circular Bio-based Europe (CBE) joint undertaking and the Engineering Biology Research Consortium (USA). These partnerships hold in common the fact that they **bring together public and private stakeholders** within consortia that are funded using a 'blend' of public funding (international, national or local funding authorities) and industrial financing. Behind the term PPP, it is possible to identify different arrangements (see box below).

### Examples of PPP Observed in the Biotechnology Domain

**TWB** (Toulouse White Biotechnology) is a research infrastructure operated by public agencies (INRAE, CNRS and INSA Toulouse) that have entered a PPP with a range of private sector stakeholders, including SPEs, large industry and financial investment companies. The PPP financially supports the operation of TWB and funds pre-competitive research projects.

**BPF** (Bioprocess Pilot Facility) and AlgaeParc (light-based bioprocesses), both located in the Netherlands, are PPP (industries, universities, and RTOs) specifically designed to enable the transition from laboratory to industrial scale. Companies and knowledge institutions can combine separate production technologies to investigate and develop their own processes.

**CBE** is a Joint Undertaking (CBE JU). This PPP involves the EU and the Bio-based Industries Consortium (BIC). The latter is a cross-sector assembly of industrial members and a range of associate members, including public research organisations, private banks, professional associations etc. BIC develops a strategic agenda that is executed within the framework of the CBE JU.

**EBRC** is a non-profit PPP funded by US government agencies and an array of industrial sector organisations. The PPP is mainly focused on agenda setting, performing roadmapping exercises and promoting biotechnology in education and regarding policymaking.



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## Biotechnology Infrastructure Business Models

**Many infrastructures only focus on certain aspects** of the biotechnology value chain.

Biofoundries automate bioengineering operations, applying the design-build-test conceptual framework to build microorganisms tailored for specific purposes. Biofoundries rely on the availability of synthetic DNA, hence the Biotechnology and Biological Sciences Research Council (BBSRC)'s strategy of creating so-called 'gene mills' that provide DNA bioparts for synthetic biology. Other RI focus on analytics, biobanks or repositories, whereas another group of RI is specifically designed for the purpose of upscaling bioprocesses, including process design and optimisation, scale-up and downstream processing. This subdivision of tasks is logical because the skills involved are quite different. Biofoundries intensively mobilize skills in biosciences and digital technologies, while the upscaling phase is the realm of chemical engineering. However, in terms of efficiency, this division of labour is suboptimal because it encourages a **silos approach** to bioprocess development and **discourages bidirectional knowledge flow** between the different development phases.

**Regarding the missions** accomplished by RIs in biotechnology, three main activities are identified: the **support of cutting-edge R&D** that irrigates the infrastructure and contributes to the permanent improvement of its services; the **production of services** to support external user projects; and the **development of products** using bespoke technology or targeting specific markets. Another differentiating feature of RIs is their customer profile. Clearly, some RIs are geared towards supporting academic researchers, while others are focused on private sector clients, from start-ups and SMEs to large industrial groups. In terms of translational research, the risk of excessive customer polarization is that **RIs are either disconnected from industrial realities or, on the other hand, deprived of high-level science.**

Since the beginning of the 21st century, empowered by new knowledge from systems biology and the onset of synthetic biology, biotechnology has become one of the fastest-growing technology areas, both in terms of innovation and economic growth. **Investments** driving this boom are provided by **private capital and government funding**. In the field of RIs, the **balance between these two financial sources** largely determines the business model. Many RI facilities are non-profit organisations that are invested with social and environmentally oriented missions (e.g. develop technologies for a carbon neutral economy). Typical examples of such RIs are DTU Biosustain, which receives funding within the framework of a PPP involving the Novo Nordisk Foundation and a public university, TWB and the two American distributed research infrastructure, Agile Biofoundry and BIOMADE USA. On the other hand, several profit-making companies, such as Ginkgo, Amyris and Zymergen have occupied the RI service provider space. These companies used private financing to massively invest in capital expenditure (CAPEX) and to recruit top-level scientific skills. However, in this case, the sheer size of the investment has influenced the business model, moving activities towards the development of products rather than RI services.



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In terms of **application areas**, biotechnology provides technologies for many market segments including energy, chemicals, materials, molecules for the agri-food sector, cosmetics, medicines, and pharmaceuticals. While many of the technologies are generic, it is obvious that each market segment requires specific equipment and know-how and involves different market players. For this reason, highly flexible, multi-sector RIs that produce an extensive range of cutting-edge services are very rare. Moreover, considering that the R&D phase in innovation pipelines is usually lengthy, costly and uncertain, it is defined as a **high risk – high gain** activity, meaning that the requisite business model is difficult to establish.

Non-profit organisations that receive public funding benefit from the fact that they can assume a certain **degree of risk** and operate within longer timeframes. However, their business model must integrate public interest services (e.g. education, outreach, focus on societal challenges etc.) and be compliant with regulations regarding the use of public funds and the valorisation of results (e.g. Europe's Open Science policy). When non-profit organizations receive funding from private sources (e.g. a foundation), their **degree of freedom to operate** is considerably increased compared to public counterparts, meaning that they can focus on the fulfilment of a public interest mission, while avoiding market pressure and the constraints of certain public regulations. Nevertheless, RIs operated exclusively by foundations, such as the BioInnovation Institute Foundation are extremely rare. The business models of for-profit organisations are necessarily dictated by the expectations of their investors. These organisations serve their customers by selling a product or service that adds value to the client's business, with incomes serving to operate and maintain the RI and remunerate shareholders or the owners. Therefore, **return on investment (ROI)** is an important metric, used to monitor investments and judge the performance of service-providing RIs. Ultimately, the ability of profit-making RIs to remain at the cutting-edge of R&D will depend on the **financial ability of the shareholders to engage long-term investment and the ability of the RI to sustain the delivery of unique, highly advanced services or products that provide a considerable competitive edge to clients.**

In conclusion, in the field of biotechnology the **ideal business model for a RI** is one that:

- **Secures the engagement of a large academic community.** This is vital to ensure that the RI is constantly irrigated with high-level science and innovation.
- **Brings together all disciplines** (especially life sciences, computer science and chemical engineering) required to deliver bioprocesses. This inevitably leads to the conclusion that the ideal RI adopts a distributed organization drawing on the high level of specialization of individual facilities embedded in disciplinary environments.
- **Offers integrated services that result from the seamless interlinkage of individual services** provided by single-site specialised facilities. The added value is greater than the sum of the component services.



- 
- Provides the basis for **strong cooperation and integration** of distributed facilities across Europe.
  - A **shared business framework** that supplies the basis for service integration and the operation of flexible, interoperable, multi-service workflows, built on the multidisciplinary nature of the RI's facilities (and whilst ensuring some degree of technical redundancy).
  - Ensures **one-stop, easy access** and business development for users requiring access to all phases of bioprocess development.
  - Operates using a **funding framework that secures long-term access to the cutting-edge science** present in universities and other public-funded research and technology organisations.
  - Strongly **engages** Member Countries to ensure that transnational cooperation remains a priority to deliver European ambitions.
  - **Mobilises** a diverse community of users/clients from public and private sectors, ensuring that its activities are both founded on the best science and driven by the most relevant and up-to-date market intelligence.

Considering these criteria, the strategic position of biotechnology in national and continental economies and the early stage of growth of biotechnology and the development of synthetic biology, **public funding** must play a significant role in supporting RIs operating in the biotechnology field. In the context of **promoting the circular bioeconomy transition**, this appears rather logical, especially if one considers that the fossil (oil, gas, and coal) industries continue to receive public subsidies, despite the well-established negative impact on climate change and environmental degradation of fossil resources. Moreover, it is evident that RIs must find a fine **balance between scientific excellence and focus on innovation and societal challenges**. Finally, the biotechnology field will be best served by the development of distributed RIs displaying the ability to combine skills and disciplines and cover a wide range of commercial sectors.

Regarding the specific context of the EU, it is obvious that there is a **need to aggregate the public investments in biotechnology**, made at the national level, to **create a distributed research infrastructure that can achieve international status**. For this, European funding is required to top-up national funding, providing the means to create and partly sustain a biotechnology-focused distributed research infrastructure able to fulfil a public mission, providing solutions to societal challenges, engaging in the education of Europe's next generation of biotechnology professionals and supporting economic development throughout Europe through the production of high-level services to industry clients.



# IBISBA, a Unique Distributed European Research Infrastructure for Biotechnology

Addressing a gap in European biotechnology, IBISBA's mission is to provide **world-class cutting-edge research and innovation services** enabling the development of biotechnology as a technology cornerstone of the circular bioeconomy. To achieve this, IBISBA integrates Europe's leading public-operated research infrastructure facilities into a coordinated business environment.

## IBISBA's Strategy

IBISBA's strategy is to **develop new science concepts, tools, and methodologies** to underpin the production of modular, interoperable services that are interlinked in workflows to support the seamless development of bioprocesses. To develop its ability to perform integrated translational research and create added value, IBISBA builds on three key pillars:

1. **A large multidisciplinary community** of leading biotechnology experts. The activities of IBISBA's specialists and their interactions with IBISBA's user community confer the scientific excellence and industrial awareness necessary to irrigate and constantly improve IBISBA's services.
2. **A range of cutting-edge technologies** built around an array of top-class equipment, tools, and methodologies, supported by a diverse portfolio of national and European funding.
3. **Advanced business practices**, digital tools and disruptive concepts for translational research that empower the operational viability of a network of facilities and provide the basis for seamless multiservice support to client projects.



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As a European distributed research infrastructure, IBISBA goals are:

- **To integrate a pan-European community of stakeholders** committed to the development of biotechnology as an enabling technology for the circular bioeconomy.
- **To achieve international recognition** as a world-class research infrastructure producing novel science and technology concepts, methods, tools, standards, and expertise capable of supporting the development of biotechnology, working with all relevant stakeholders to achieve this.
- **To develop unique operational capabilities**, built on shared business practices and standardization, designed to deliver seamless modular service workflows.
- **To contribute to the development of biotechnology** through the provision of a variety of FAIR data assets, including protocols, workflows and models, brought together in a knowledge commons.

## IBISBA's Value Proposition

### Who Will IBISBA Target?

As a pan-European research infrastructure, IBISBA supplies scientific research services and creates added-value to a wide variety of **stakeholder groups**:

- Its own network of research facilities, present in **national nodes**
- **All R&D&I players** involved in biotechnology, whether in academia or industry requiring access to research infrastructure and advanced modular services
- **Public authorities**, funders, and policymakers

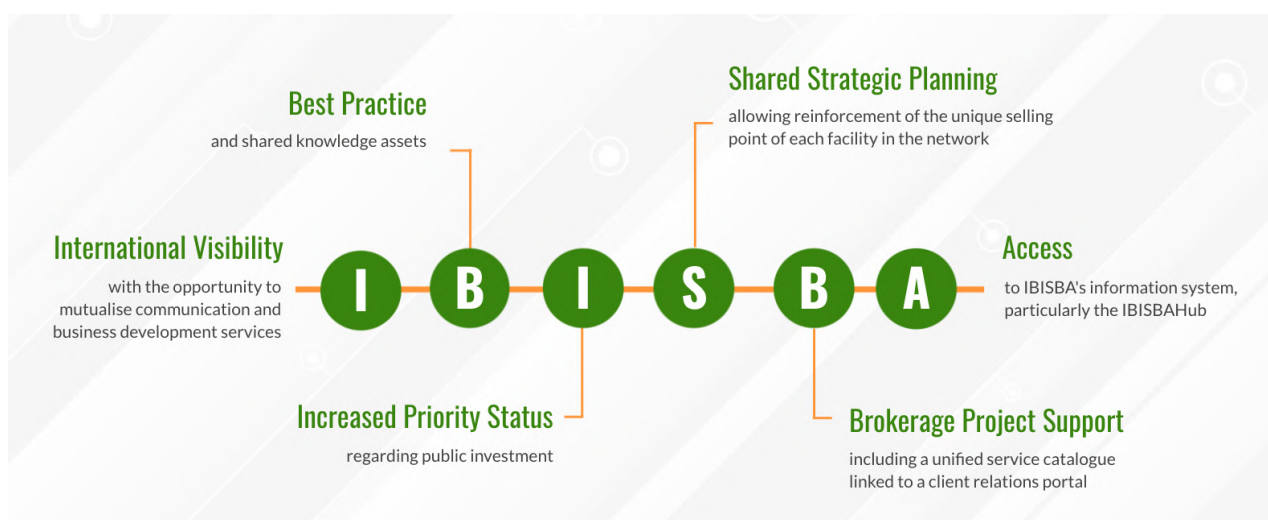
### Facilities Within National Nodes Providing Added Value to Enhance the Impact of a Distributed Research Infrastructure

IBISBA strengthens the synergies among RI localised in different member countries. It does so through enabling a (centrally managed) network of facilities, whilst deploying workflows that enable seamless, flexible and modular operation among them. This creates a **distributed research infrastructure** enterprise characterised by the following features:

- **International-level visibility** gained through mutualised communication and the ability to engage in international cooperation activities, working with similar national or multinational organisations.
- **A common service access** interface (one-stop-shop) for users, supported by mutualized business development and client relations management capabilities.



- **Shared business practices**, standards, and knowledge assets, providing the basis for integrated services delivered to users in the form of modular service workflows.
- **Business processes** and project monitoring capabilities embedded in an IBISBA-specific cloud-based information system.
- **Shared strategic planning**, allowing reinforcement of the unique selling point of each node and each facility in the network, identifying where duplication is necessary to meet demand and where it is unnecessary.
- **Maximum visibility** with regards to European, National and Regional policymakers and public funders.



## The Global Community of Biotechnology Researchers - Enhancing User Experience and Offering New Services

The primary user/client of IBISBA's experimental services are R&D&I players operating in different public and private industry sectors. This target group benefits from:

- **A single-entry point** to access to a wide range of modular services offered by leading research infrastructure facilities across Europe. Materialized by a web portal and catalogue, the one-stop-shop offers IBISBA users fast track access to a rich range of services and expertise.
- **An efficient client interface** minimizing business transactions and shortening timelines. This may include service-level contracts that will confer IBISBA with the ability to act on behalf of its facilities and straightforward, transparent IPR management.
- **Access to a range of modular services** that can be assembled into client-specific project workflows.
- **Real-time project monitoring** and final project reporting.
- **Distant and onsite training** in various areas of biotechnology.
- **Access to a data registry** where project data assets are registered and shared, offering a simple means to FAIRify data. IBISBAHub users can opt to maintain full confidentiality, apply partial restrictions, or publicly release their assets, digitally identified using an IBISBA-specific DOI.
- **A single entry point** to a wealth of information including protocols, models, and workflows.



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## Public Stakeholders and Biotechnology Innovators - Generating Expertise, Foresight, and Support to Local Innovation

As a pan-European research infrastructure, IBISBA's expert community performs ongoing activities aimed at maintaining it at the cutting edge of biotechnology. This requires a continuous appraisal of the latest S&T breakthroughs and **foresight analyses** to anticipate developments in the field and future investment. This information is made available in the form of:

- **Expertise** regarding science and technology (S&T) advances in the field of biotechnology (e.g. foresight analyses and regular policy notes).
- **Strategic national and transnational S&T alignment**, guaranteeing “more for your money”. Optimising IBISBA capabilities is an intrinsic part of the infrastructure. Therefore, IBISBA will supply the means to guide investment, avoiding unnecessary expenditure while pinpointing technologies that require reinforcement and even duplication across Europe.
- **Interregional coordination** to support sustainable smart specialisation strategies and pan-European support for local enterprises. As a distributed research infrastructure, IBISBA is grounded in Europe's regions, particularly those where biotechnology is identified as a leverage for innovation and economic growth. Through its cooperative network, IBISBA is an intermediate to link local innovation initiatives, offering SMEs pan-European access to biotechnology.

## A Consistent Value Proposition to Promote Biotechnology in a Challenging Context of Transition

The **proposed business model for IBISBA** confers the research infrastructure with the ability to provide unique support to research and innovation projects in the field of biotechnology. Bringing together a group of leading European biotechnology experts and first-class research infrastructure, IBISBA creates the conditions for accelerated research and innovation. Using advanced digital technologies, IBISBA overcomes the drawbacks of distributed infrastructure, crossing national and disciplinary frontiers using structured business processes that ensure **timely project execution, quality control and project auditing**. In this regard, IBISBA strengthens Europe's research position in biotechnology and promotes innovation.

The timely implementation of IBISBA will form a vital **steppingstone** in Europe's quest to become a **world leader in climate action**. IBISBA supports research and innovation in a variety of climate-relevant application areas, having demonstrated its ability to support the production of biofuels (e.g. ethanol and biokerosene), fine chemicals (e.g. isobutene and itaconic acid for the polymer industry), food and feed components (e.g. aromatics, nutrients, etc.), amino acids (e.g. L-phenylalanine), biologicals (e.g. monoclonal antibodies) and the development of enzymes and microorganisms to deliver services, such as plastics (PET) recycling, CO<sub>2</sub>-capture and biocontrol in agriculture. Most recently, some facilities in IBISBA have contributed to research efforts to combat the Covid-19 pandemic, producing for example viral antigenic proteins, and developing cell factories for vaccine production.



# Achievements and Status of IBISBA

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Since its early beginnings in 2014, the IBISBA concept has progressively taken form, arriving at its current state of preparation. Progress has been sustained by support from research facility owners (RTOs and universities), national funding sources and two European-funded projects [6] and the funding attributed to facilities present in emerging national nodes. Moreover, additional impetus has been provided by the inclusion of IBISBA on the ESFRI roadmap, this being effective since September 2018. Within ESFRI, IBISBA is most connected to the **Health & Food strategic working group**, although its services are also relevant to the **Environment** and **Energy strategic working groups**.

## IBISBA is Present in 9 European Countries

Currently, IBISBA gathers research facilities owned by RTOs and universities from 8 EU member countries (France, Spain, Italy, The Netherlands, Germany, Belgium, Greece, Finland) and the United Kingdom. By fostering their integration, IBISBA uniquely produces translational R&D&I services for an international community of biotechnology stakeholders. IBISBA aggregates expertise from different scientific domains and simplifies access to advanced multidisciplinary services to accelerate end-to-end bioprocess development. In doing so, IBISBA contributes to the delivery of low carbon, low environmental footprint technologies for a wide variety of market sectors.

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[6] IBISBA receives funding from the EU's H2020 research and innovation programme under grant agreements No 730976 and 871118. IBISBA 1.0 is a H2020 INFRAIA starting community project that began December 2017 and will terminate in May 2022. PREP-IBISBA is a H2020 INFRADEV Preparatory phase project that began in January 2020 and will finish in December 2023.





Figure 2 - IBISBA's founding partners are present in eight member states and the UK.

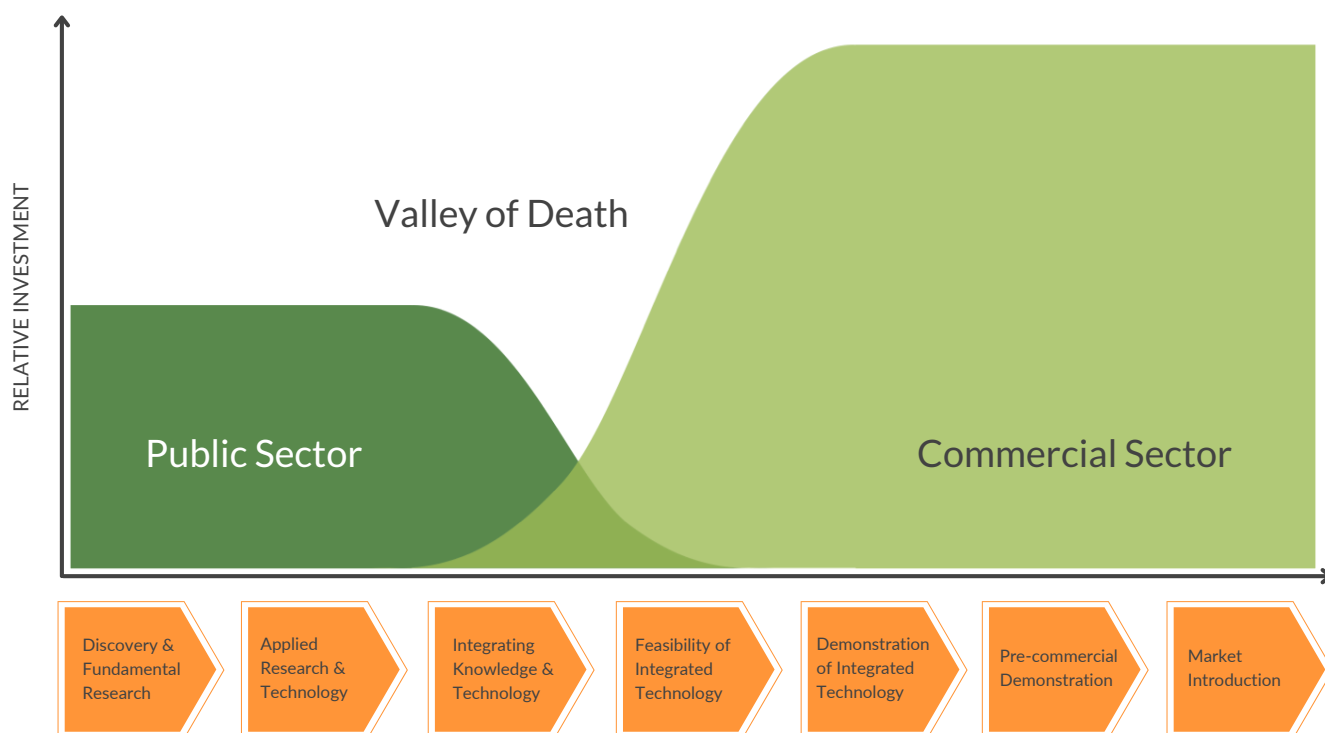
## Defining IBISBA's Uniqueness Among European Life Science Research Infrastructure

Reports published by the OECD and other organisations, as well as the expert opinion of the European Strategy Forum on Research Infrastructures (ESFRI), recall that large research infrastructure and distributed research infrastructure play major roles in science and innovation ecosystems. In the life sciences, the European landscape is well populated by a range of infrastructures, some of which figure on the ESFRI roadmap under the Health and Food classification. Within this subgroup, most of infrastructures focus on disciplinary science. For example, INSTRUCT-ERIC successfully integrates a whole range of services in the field of structural biology (X-ray diffraction, NMR, electron microscopy etc.), while the more recent ESFRI project EMPHASIS focuses on plant sciences, specializing in plant phenotyping and in-field trials. In the biomedical field, EATRIS adopts a multidisciplinary science approach to tackle drug, vaccine, and medical diagnostics development, moving innovation upwards along the TRL and MRL scales [7]. However, multidisciplinary infrastructure addressing technology issues related to the circular economy are rare. Indeed, this is one reason why the new Horizon Europe framework programme is encouraging the **creation of multi-infrastructure consortia to tackle grand societal challenges**. In the context of European ambitions, such as the Green Deal, ensuring infrastructure support for **translational research** is a clear signal that Europe's research infrastructure stakeholders must fully embrace.

[7] S. Petrovic and E. Hossain, "Development of a Novel Technological Readiness Assessment Tool for Fuel Cell Technology," in IEEE Access, vol. 8, pp. 132237-132252, 2020, doi: 10.1109/ACCESS.2020.3009193.

## Redefining the Term Translational Research

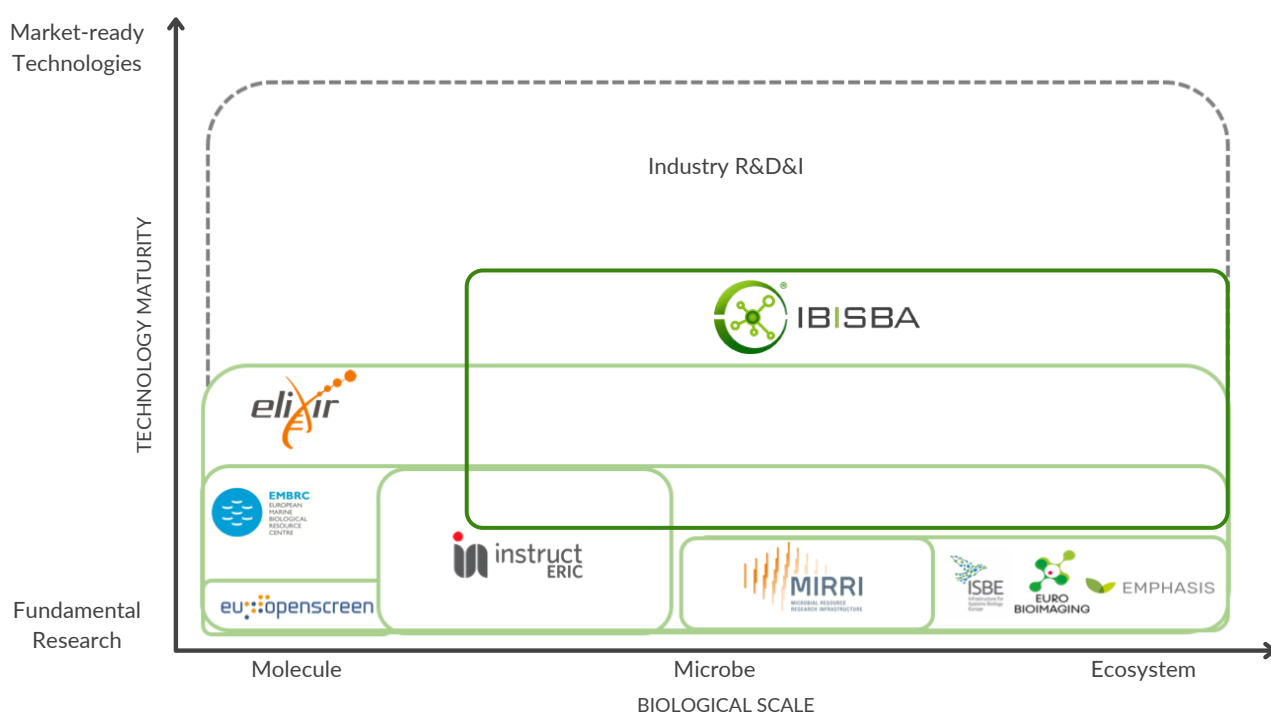
The term translational research is synonymous with bench-to-bedside medical research. However, strictly speaking, it describes a more generic concept of research and innovation process that uptakes fundamental research knowledge generated at the laboratory level, moving this towards innovation and application in transdisciplinary contexts involving other non-scientific stakeholders, including the user or consumer. Importantly, translational research is also a bidirectional process, which captures knowledge specific to the application domain (e.g. process or logistics constraints), driving this back into research activities targeting the integration of technology bricks to build prototypes and perform feasibility studies. Importantly, translational research can help to bridge the so-called valley of death, which is that part of the innovation trajectory least well invested by the public sector and not yet completely invested by private industry.



**Figure 3** - The innovation valley of death. This well-known phenomenon arises from the fact that public research rarely extends beyond the laboratory scale, focusing mostly on fundamental research, while industrial R&D mostly invests the latter stages of the TRL scale, notably levels 5-7. This means that early innovation is less the focus of both the public sector and private industry.



In this regard, **IBISBA is a highly relevant addition to the ESFRI family.** This is because IBISBA is designed to support translational research and innovation within the framework of the circular economy, addressing a whole range of market sectors and societal challenges that are relevant to Europe's Green Deal policy. Within the ESFRI landscape, IBISBA is well positioned to draw upon fundamental scientific research and research services provided by infrastructure such as ERIC-INSTRUCT, MIRRI, EU-OPENSOURCE etc. using this to perform more applied and integrative research and development work. The overarching aim of IBISBA is to support translational research providing the scientific and technical resources to design and build different technology bricks and begin to integrate these into processes that can be tested at pilot scale before handover to industrial R&D for further development towards market implementation.



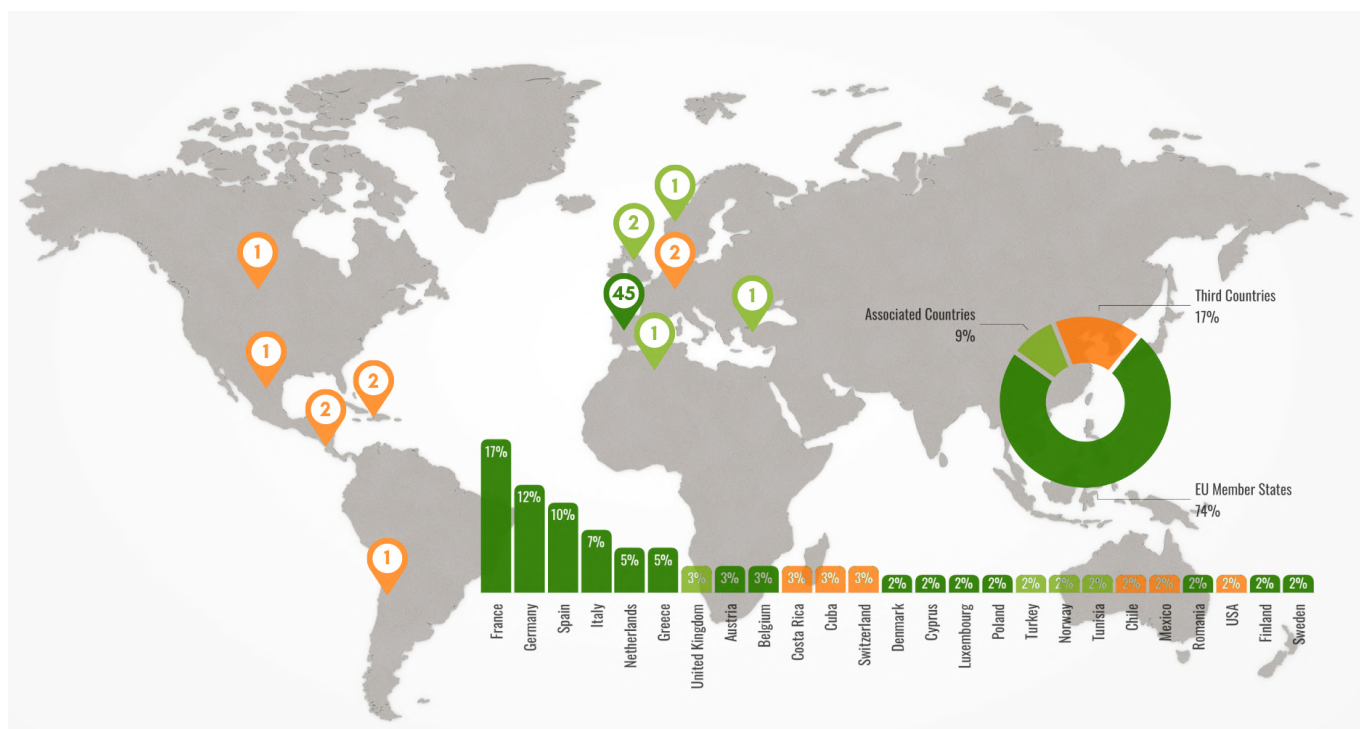
**Figure 4** - ESFRI operating in the circular economy. Different ESFRI are positioned according to their potential contribution to R&D&I related to the circular economy, taking into account the technology maturity level and biological scale.

## Achievements and Progress Towards Implementation of IBISBA

Beginning in December 2017, the Horizon 2020 INFRAIA starting community project IBISBA 1.0 has provided IBISBA's stakeholders with the opportunity to work on many features of the future IBISBA research infrastructure. The **achievements of this project** are numerous, but several outcomes highlight in exemplary manner progress towards implementation of IBISBA.

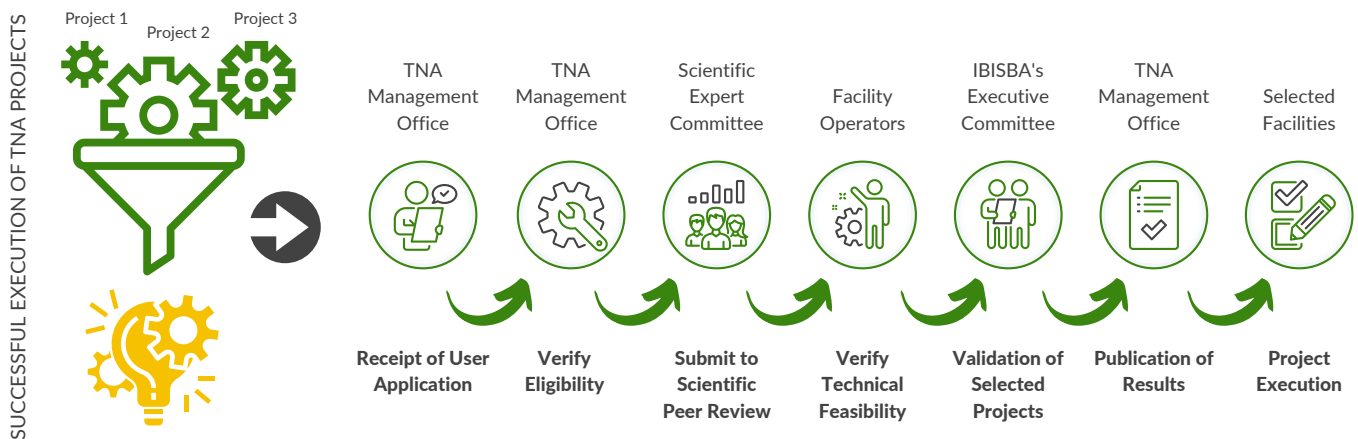
## Transnational Access

Since 2019, using funding from the European Union’s Horizon 2020 framework programme, IBISBA has launched 6-monthly calls for subsidized access to its integrated services. This **highly successful pilot scheme** provides the means to realize goals of the European research area, supporting researcher mobility and democratizing access to cutting edge research infrastructure across Europe. So far, the program has **successfully supported researchers from both academia and SMEs**. Additionally, the transnational access program serves as a platform for international visibility, supporting research projects emanating from third countries.



**Figure 5** – Transnational access operated by IBISBA. As of 2021, five calls for transnational access have been launched and 59 user access projects received. Most projects are from European Member Country-based academic groups, but SMEs are also well represented. Importantly, some user access projects are from third countries.

The operation of transnational access relies on a carefully designed process that delivers clear guidelines to users and transparency throughout the selection procedure. Projects are primarily selected based on scientific excellence, but are also screened for technical feasibility and, when relevant, potential socioeconomic impact. The latter criterion is particularly important to screen projects from private industry (mostly SMEs).



**Figure 6** – A Knowledge commons to raise capability across facilities and across participant member countries. TNA is transnational access.

Early transnational projects generally involved the delivery of services provided by single facilities. However, more recent TNA projects have provided the opportunity to develop IBISBA's ability to integrate services and develop modular project workflows. Currently, the TNA programme is geared towards the **production of services in the form of modular project workflows** and this criterion has been added to the selection criteria, meaning that single service requests are now considered lower priority, because they offer less added value.

### One-stop-shop Access to IBISBA Services

A key early achievement has been the **development of a complete catalogue of services** and the creation of a web portal for IBISBA clients. The catalogue contains a whole range of services that are organized in a way that simplifies consultation. It is available at IBISBA's web-based service portal (<http://ibisba-services.eu/>). Clients can browse services, selecting them to generate a client-specific list that can be submitted to obtain more information. Client contacts are currently being dealt with by a business development team composed of business developers working for IBISBA's participant stakeholders.

## IBISBAHub: An IBISBA FAIR Data Registry and Portal

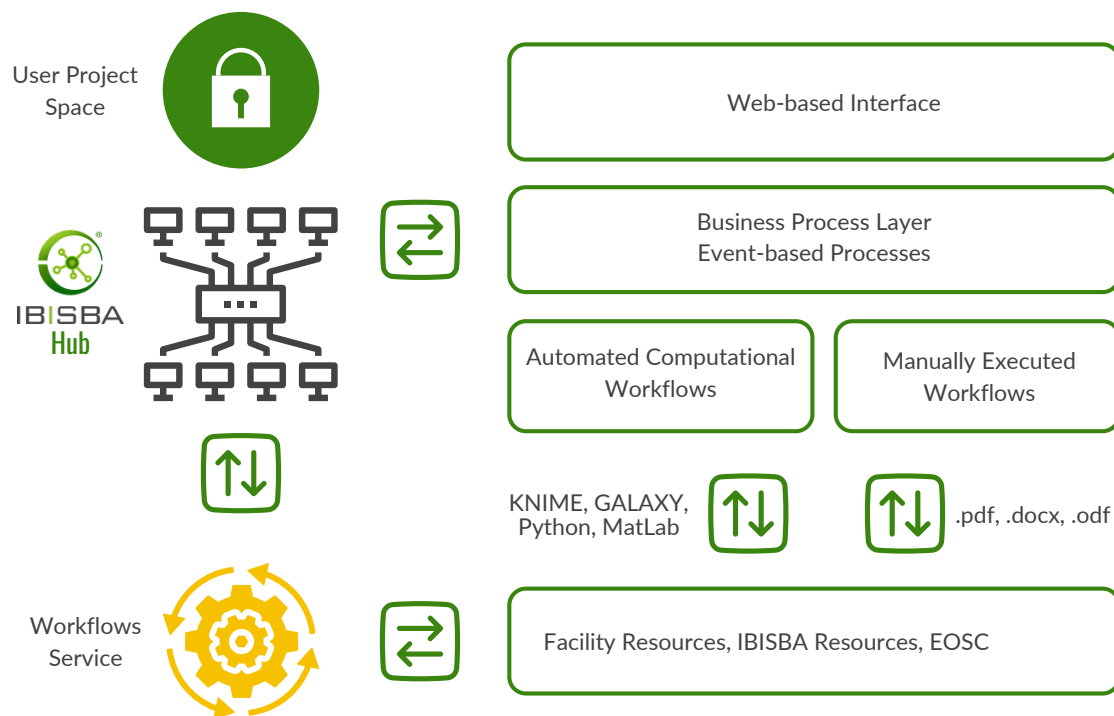


Figure 7 – A Knowledge commons to raise capability across facilities and across participant Member Countries.

The so-called IBISBAHub (<https://hub.ibisba.eu/>) is a shared space for recording, accessing, and sharing data assets of the IBISBA project. It is a customised and extended installation of the FAIRDOME SEEK asset management platform [8]. The IBISBAHub provides an online portal that opens access to a variety of services:

- **Self-manage** project assets, organising, sharing, and disseminating assets arising from multi-partner collaborations, as well as project events
- **Manage** data resources, using IBISBAHub either as a primary user management resource, or as a complement to local resources
- **Store, register, share** and/or access standardised protocols, computational workflows and data format templates
- **Describe and inter-relate** data assets using rich metadata relevant for samples, organisms, models, protocols, data, and documents
- **Integrate** with third-party tools, such as modelling tools (e.g. JWS Online), metadata capture tools (e.g. Rightfield) and development repositories (e.g. GitHub)
- **Report** on projects, using the IBISBAHub contents as raw material to compile reports.

[8] <https://seek4science.org/>



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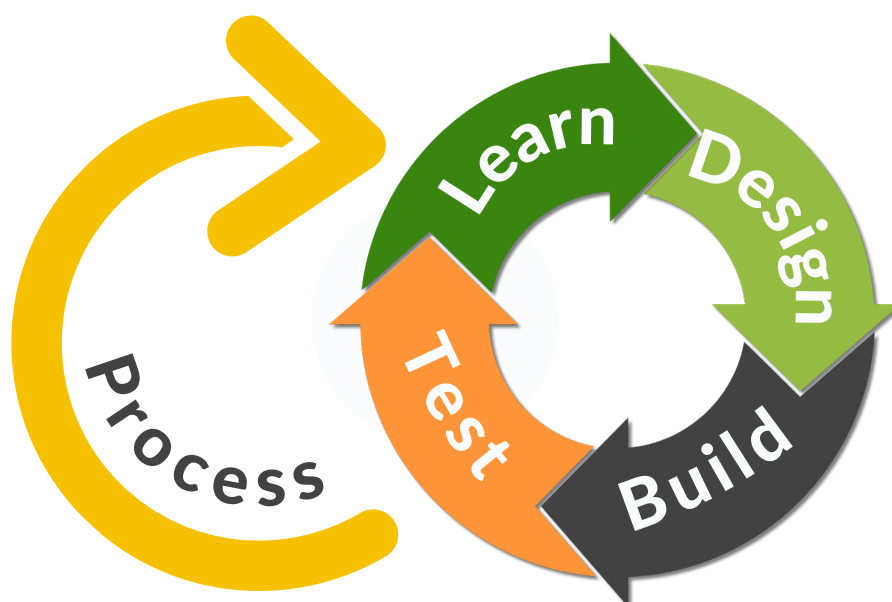
## The IBISBA Handbook

The use of the IBISBAHub is supported by a **comprehensive handbook** (<https://ibisba.github.io/handbook/index.html>) that supplies all necessary guidelines. Additionally, as a public information resource, the handbook provides a wealth of information on IBISBA to both its members and IBISBA's user community. The Handbook also contains practical instructions on how to write and curate protocols.

Because IBISBA provides its experimental services in the form of **modular project workflows**, the handbook contains general guidelines and practical how-to instructions. Resources available in the handbook include videos, related to the different parts of the project life cycle, and supporting sections explaining harmonization/standardization, including terminology, protocols/metaprotocols, and workflows. The latter category includes automated computational workflows.

## Building a Framework for Shared Research Workflows

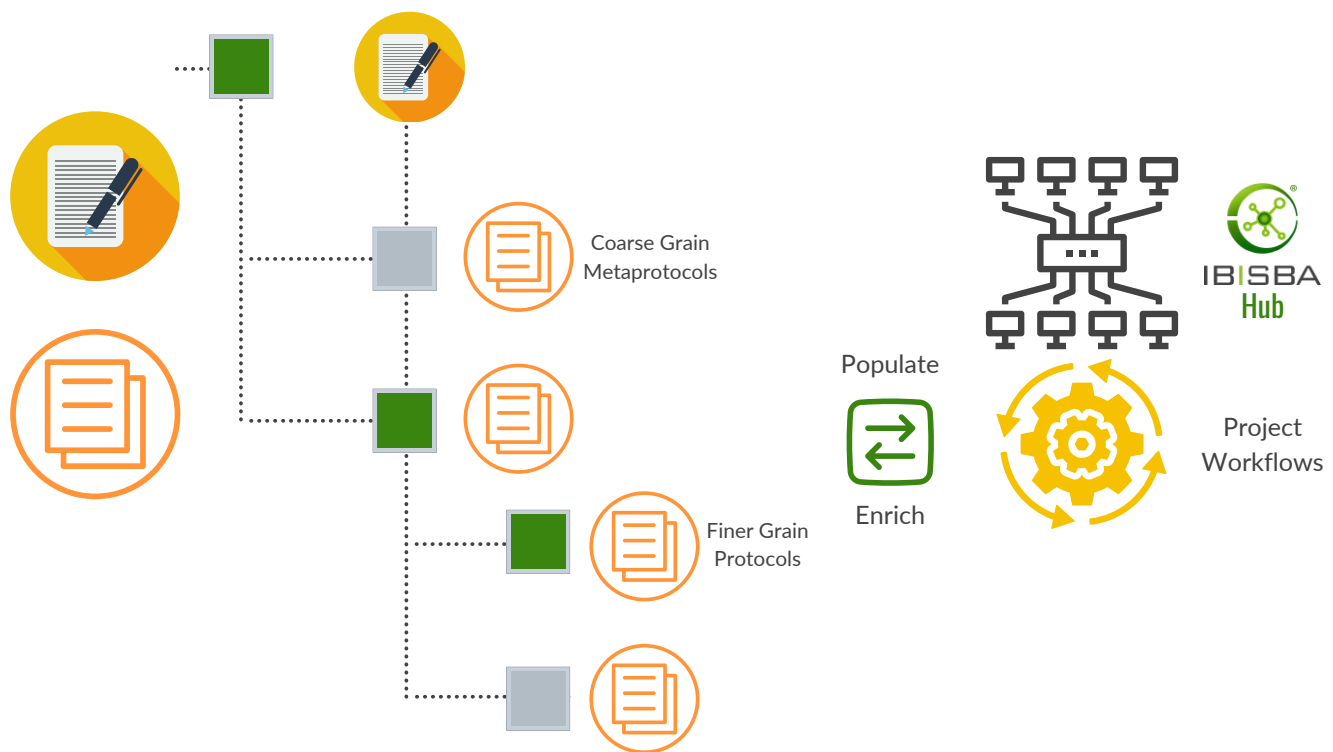
To accelerate bioprocess development, IBISBA aims to seamlessly interlink different facility-based services, embedding these in modular workflows that will support the execution of user projects. To achieve this, IBISBA researchers are using a modified form of the design-build-test-learn (DBTL) cycle that has become a hallmark of synthetic biology applied to production-based processes.



**Figure 8** – Adapting the DBTL conceptual framework for bioprocess development. In synthetic biology “build” refers to the construction of enzymes or microorganisms, whereas IBISBA includes the process scale, optimizing integration of the (optimized) biocatalyst into a bioprocess environment. This modified concept is referred to as DBTL-P.

In the framework of the Horizon 2020 project IBISBA 1.0, the work of **modularising the DBTL-P** platform has been initiated, creating a purpose-built digital tool known as “TasCu” or task curator. Using the DBTL-P framework, this tool creates an organised hierarchical list of operations, which define each phase in the DBTL-P cycle. The tool is interoperable with IBISBAHub, meaning that the projects within the IBISBAHub environment can be populated with information from TasCu, with TasCu operations being mapped to steps in the IBISBAHub.

To test the **operational relevance** of IBISBA’s DBTL-P concept framework, a case study is underway that focuses on the bioproduction of an industrially relevant platform chemical. The aim is to design, build, test and optimise two microbial strains (the yeast *Saccharomyces cerevisiae* and the bacterium *Pseudomonas putida*) to carry out a relatively well-established biobased process.



**Figure 9** – Building a framework for modular workflows integrating IBISBA services. Powerful digital tools such as TasCu and the IBISBAHub, as well as relevant standards and shared best practices, form the basis for seamless bioprocess development carried out between several facilities.

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## Training and Expertise

Seamless operation of very diverse, high-quality equipment in facilities across Europe working together in cutting-edge, multidisciplinary research projects requires not only **specialised training** for the dedicated facility-bound operators, but also a **common understanding** of the underlying (meta)protocols, workflows and processes by facility managers, operators, and users. Therefore, IBISBA 1.0 has made substantial efforts to:

- Develop a **common scientific and technological culture** and exchange good practices among the multidisciplinary project beneficiaries
- Develop and deliver **e-learning** and face-to-face training to infrastructure operators (current beneficiaries and external)
- Provide and coordinate **training** for potential infrastructure users
- Build **skills in accessing and sharing** knowledge with other research groups, especially from groups in other disciplines
- **Familiarise** stakeholders with modelling, systems technologies, aids and tools as they are required to integrate tasks, reduce development times, and automate manual pieces of work

These efforts entail dedicated workshops (harmonization, terminology, standards, operating procedures, (meta) protocols, workflows), hands-on work on a myriad of case studies (in particular those in the scope of IBISBA's joint research activities and commissioned work through the transnational access projects), e-learning activities and training webinars.

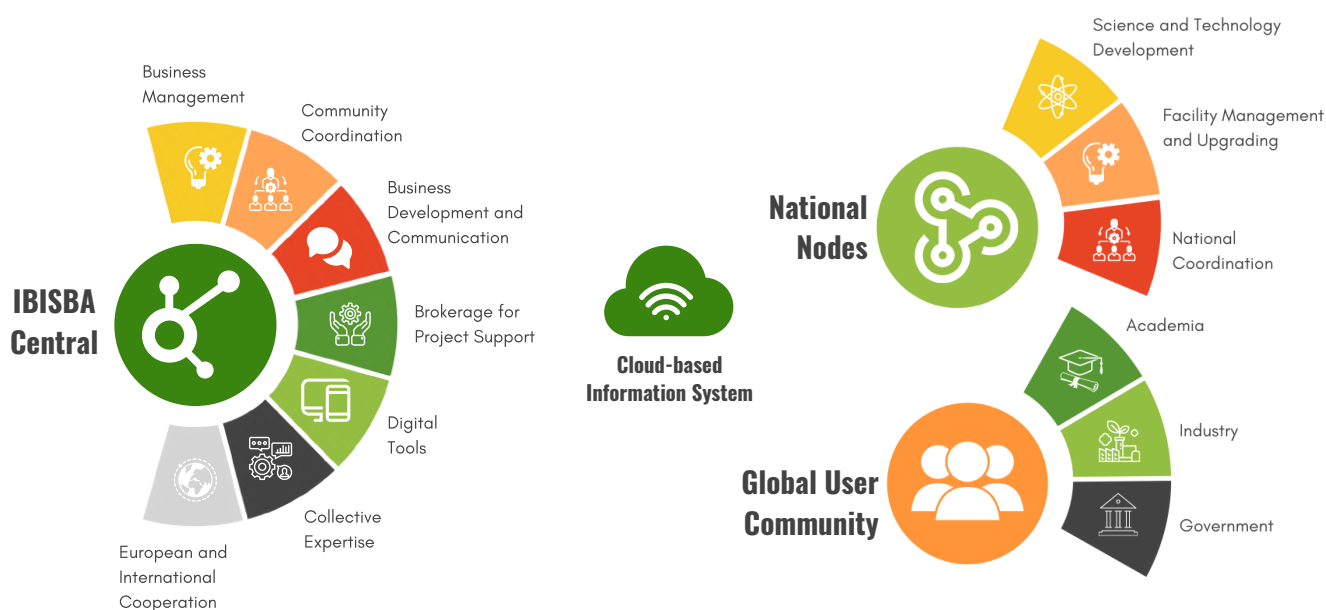


# Defining the Business Framework for Success

## IBISBA's Organisation

Early findings from work performed in the scope of the preparatory phase project PREP-IBISBA indicate that the future IBISBA research infrastructure will be organized around three pillars:

- **A distributed network** of facilities organized within National Nodes
- **A central coordination** component
- **A cloud-based information system**



**Figure 10** – IBISBA's organization. As a distributed pan-European research infrastructure, IBISBA will operate using the scientific and technical capabilities localized in national nodes. The synergy between these will be generated by the addition of a central management organization that will bring together and add value to the individual capabilities of the nodes. Linkage of the national nodes and central management will be achieved using advanced cloud-based digital technology. Finally, IBISBA will be completed by its wider user community, composed of academic, private industry and government stakeholders.

## National Nodes

The scientific and technological capabilities of IBISBA are developed within the framework of Member Country investments and local management. Most of the facilities contributing to IBISBA are identified as parts of nationally based research infrastructure that are earmarked for funding by national agencies. The owners of facilities are responsible for implementing strategy, staffing and research quality. IBISBA national nodes will adopt organizations that are best suited to the national context, thus they are likely to be configured differently from one country to another.

The primary role of National Nodes is to structure national research infrastructure in the field of biotechnology, building research service capability and interoperability, and a well-organised stakeholder community. Additionally, in the framework of IBISBA, National Nodes will endeavour to develop research service offers to IBISBA, the aim being to compile a comprehensive catalogue of top-quality integrative services for international R&D&I clients. It is expected that the different National Nodes will develop unique selling points, differentiating to some extent their service offer from those of other National Nodes in the IBISBA network.

## IBISBA Central Coordination and Management Structure

Coordination, international visibility and cooperation, and the operation of the various business practices and support systems required to implement IBISBA services are provided by a central management structure (IBISBA central). The staff appointed to IBISBA Central ensure the coordination of the network of IBISBA facilities and, in the framework of service level agreements, define the standards and practices required to produce modular services and project workflows for IBISBA. IBISBA central delivers IBISBA's communication strategy and coordinates business development activities, managing client relations. The IBISBA Central staff might also coordinate service contracts, monitoring project processes across project life cycles and handling financial affairs. Finally, as a coordination team, staff members are responsible for organizing internal training for facilities and monitoring research quality in collaboration with facility-based QEHS specialists.

## A Cloud-Based Information System

IBISBA Central and national-based IBISBA-affiliated facilities operate together using a cloud-based information system that is composed of an event-based business process layer and various digital services, including an online catalogue of facilities, a client relations management system and a data asset registry. All IBISBA operations are supported by the information system, thus ensuring transparency and traceability. IBISBA's information system is extensively connected to external resources leveraging collaborations with best in class international e-infrastructure to provide these.

## IBISBA's Governance Structure

In the framework of the Horizon 2020 project PREP-IBISBA, the future governance structure of IBISBA has been studied. This has involved benchmarking studies (including 12 research infrastructures included on the current ESFRI roadmap) to discover how other European research infrastructures are organised and governed, as well as internal consultation using surveying methods. The preliminary conclusions of this work confirm that, to achieve its goals and fulfil its mission, IBISBA must acquire legal status.

Several legal models were examined (ERCI, AISBL, GmbH, IGO etc) in the course of the work performed. This careful analysis has led to the conclusion that **the preferred model for IBISBA is an ERIC (European Research Infrastructure Consortium)**. Among the reasons for this conclusion, the following are prominent:



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- The ERIC status is most emblematic of pan-European cooperation. IBISBA is clearly anchored in a framework of **European cooperation**, thus other legal models such as national-based non-profit companies are less relevant to IBISBA's ambition.
  - The **establishment of an ERIC is relatively fast** compared to some other models, although how fast is unclear at this stage. Considerable accumulated experience of ERIC statutes among member countries has progressively increased confidence and understanding of this model. This argues in favour of a timeline that is compatible with the plan for implementation of IBISBA. Nevertheless, the time consideration is not an exclusive feature of an ERIC, because work also identified the relative simplicity, characteristic of the process required to create an AISBL Association Internationale Sans But Lucratif).
  - The **national perception** of ERICs and other legal models. Internal surveying revealed that some of IBISBA's member countries may not wish to support the creation of an entity using an alternative legal model. In many European Members Countries, ERIC status corresponds to a vision of how research infrastructure strategy is organised up to the European level. The creation of a research infrastructure using another legal status is likely to lead to a loss of government support.

One negative aspect related to the creation of an ERIC relates to the fact that this legal regime is defined by European law. The participation of associated and third countries is possible provided that these recognise the primacy of the European Union legal system and the validity of the ERIC regime. In the wake of BREXIT, there is a risk that **ERIC status will deprive IBISBA of full participation from a UK national node.**

Regarding **alternative legal models** for IBISBA, **AISBL status is flagged as suitable.** This is because AISBL status is well-known and recognised across the globe. Moreover, to some extent AISBL status is also emblematic of European cooperation, while allowing the inclusion as full members participants from non-EU countries. As a legal regime, AISBL is a quite stable association format, but dissolution is complex. This last point is problematic if the IBISBA consortium wishes to consider an AISBL as a stepping stone towards the creation of a more definitive legal structure. Moreover, it is noted that, unlike the ERIC legal regime, AISBL status does not permit VAT exemption on purchases. Finally, the AISBL legal regime is accorded by and linked to Belgian legislation, a fact that can be perceived by other countries as either an advantage or a disadvantage.



## Exploring the Governance of ERIC-IBISBA

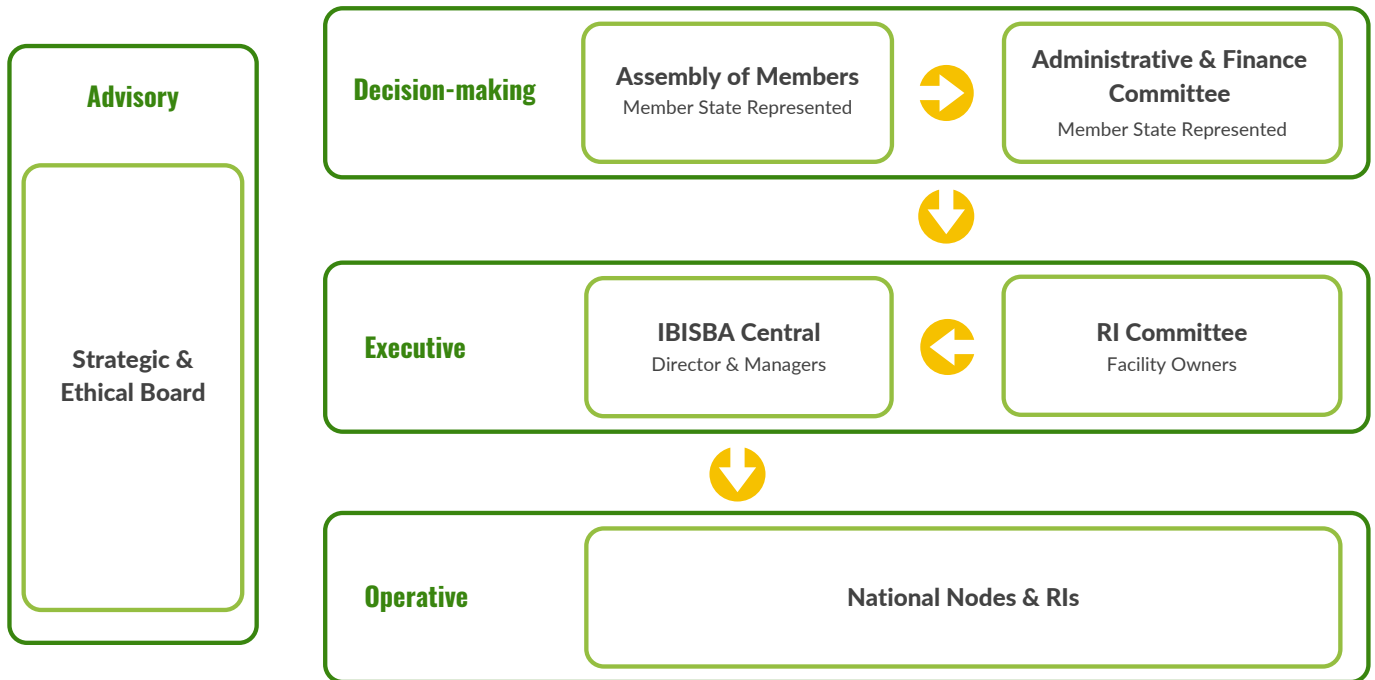


Figure 11 – ERIC-IBISBA's governance structure, composed of decision-making, executive and operative level bodies.

If IBISBA chooses to adopt ERIC status as its legal regime, the governance structure will be designed to be lean and efficient, being composed of three strata. The decision-making level will be composed of two bodies:

1. The Assembly of Members, composed of representatives of all member countries that are joint owners of ERIC-IBISBA
2. The Administrative and Finance committee, a body that is composed of ministerial representatives from participant member countries.



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The Assembly of members holds ultimate responsibility for ERIC-IBISBA. As such, it defines the budget for ERIC-IBISBA and determines pluriannual contributions from member countries. The Assembly is assisted in financial affairs by the Administration and Finance committee, composed of one representative from each member country, members being experts in administrative and financial matters. The Assembly of Members appoints ERIC-IBISBA's director and on an annual basis validates his/her strategic workplan. The Assembly also adopts KPIs used to monitor performance of ERIC-IBISBA and advocates for ERIC-IBISBA at the EU level, notably within the framework of key bodies such as EOSC, the ERIC Forum, and ESFRI. The Assembly appoints Advisory board members and monitors the overall functioning ERIC-IBISBA's governance structures. Finally, the Assembly of Members decides on the admission of new Assembly Members and validates the facilities that are eligible to produce services for ERIC-IBISBA.

At the **executive level**, ERIC-IBISBA is composed of IBISBA Central and the Research Infrastructure Committee, the latter being composed of representatives of the different research and technology organisations present in national nodes. This committee plays an important role, approving new client-oriented services, new rules, and quality requirements. It also monitors the performance of the information system and proposes improvements. Likewise, it coordinates investments across national nodes and supports the Director in workplan preparation.

The **operative level** (i.e. the level at which most external services are produced) is composed of national nodes, which are organisations based in member countries. National nodes will adopt organizations that are best suited to the national context, thus they are likely to be configured differently from one country to another. National nodes and the facilities therein produce individual service modules and contribute to ERIC-IBISBA activities. Communication and promotion of ERIC-IBISBA at the national level are mostly organised by nodes, and node chairpersons are the key contact points for Member state authorities. National nodes define science and technology development strategy, apply for funding, and implement investments. National nodes ensure that member facilities implement ERIC-IBISBA work practices and standards and propose new facilities to the Assembly of Members. Finally, in certain circumstances, members of national nodes supply in-kind contributions (e.g. staff secondment) to IBISBA Central.

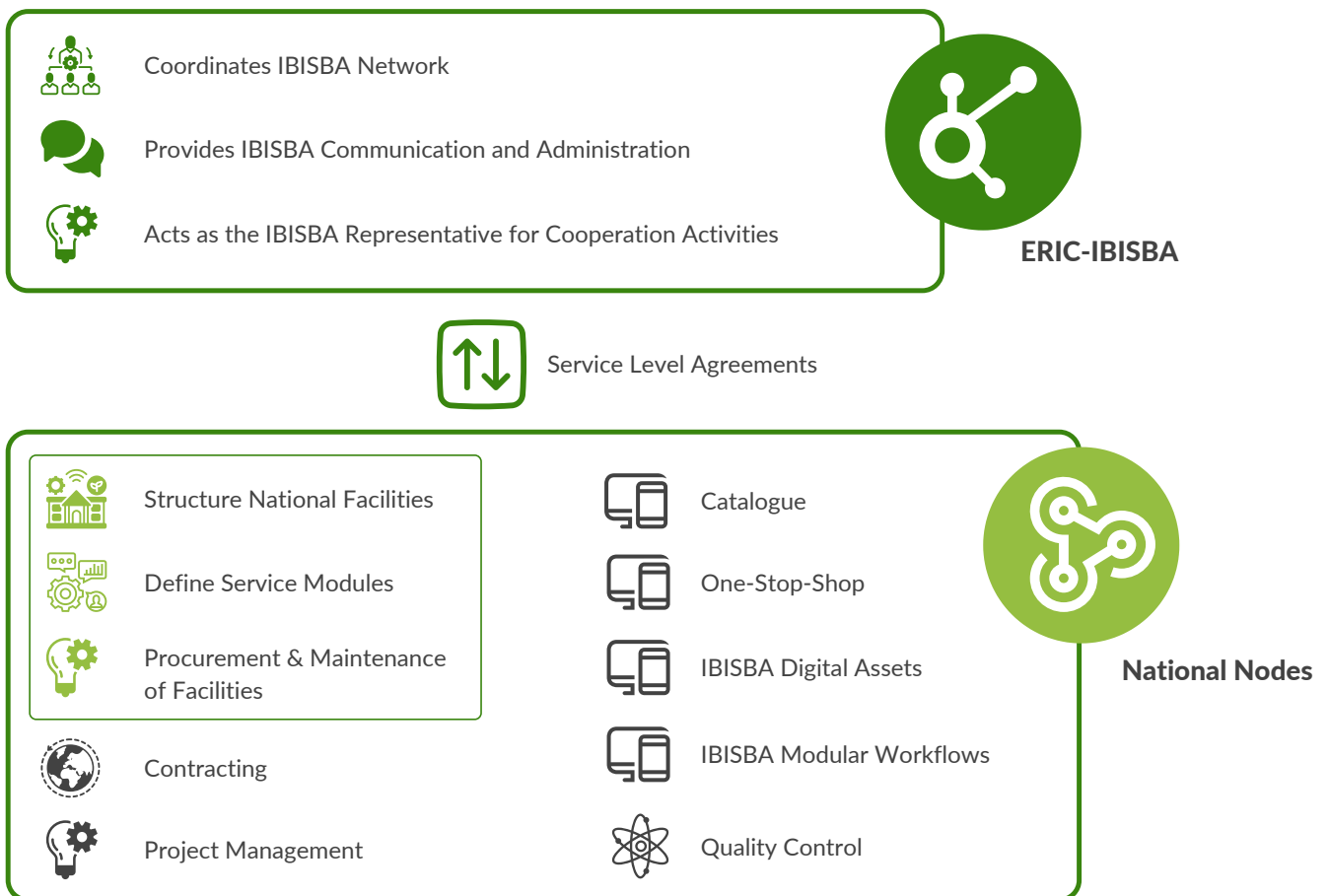
Finally, the governance of ERIC-IBISBA will be completed by **advisory boards**. Several possibilities exist (e.g. User committee, Technical committee, Industry advisory board etc.), but an essential advisory board has been identified. The **strategic and ethical advisory board** will advise on strategy related to scientific and technical issues, assisting with planning and foresight studies. Moreover, this board will provide independent periodic reports on ethical subjects, provide expertise on regulatory issues, and offer advice on social acceptability and citizen engagement related to synthetic biology and technologies for the circular economy.



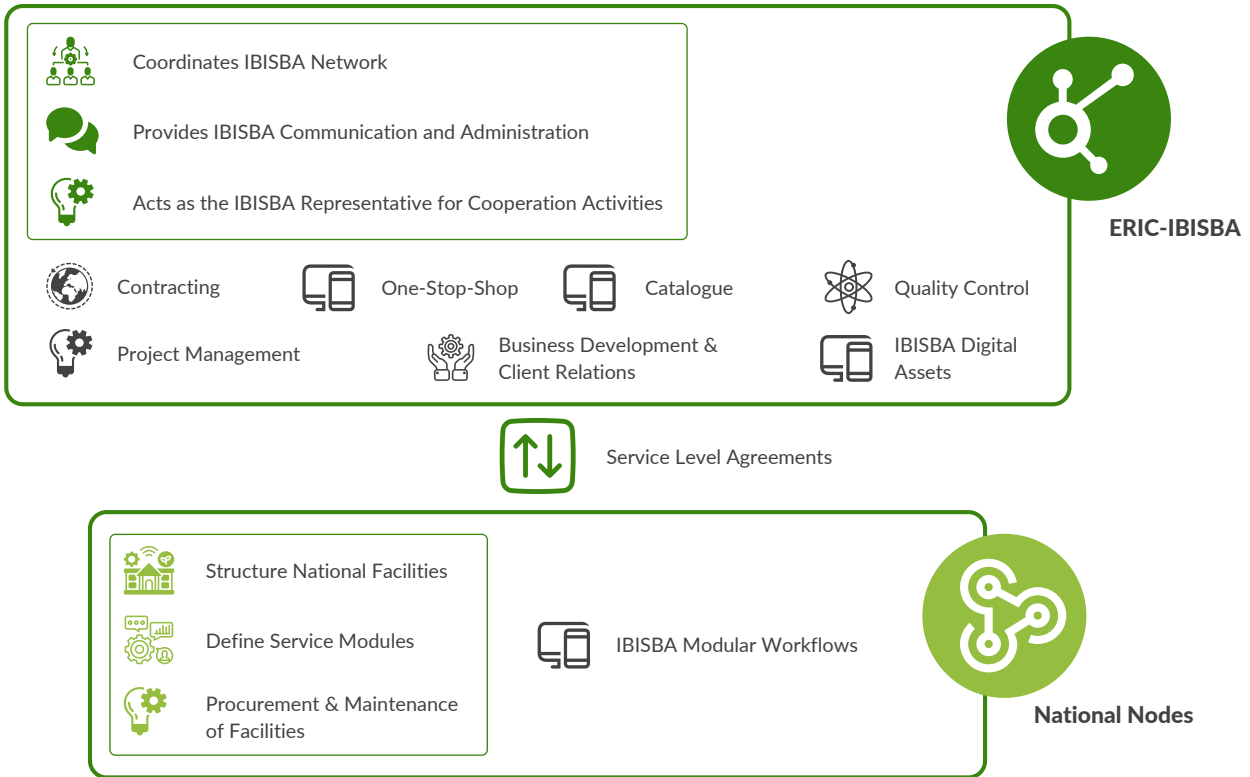
## Operating ERIC-IBISBA

The exact mode of operation of ERIC-IBISBA has not yet been defined. This means that the relative responsibilities of IBISBA central and the national nodes have not yet been fully explored and the relationship between these two entities is so far incompletely defined. Nevertheless, hypotheses have been identified and preliminary choices are possible:

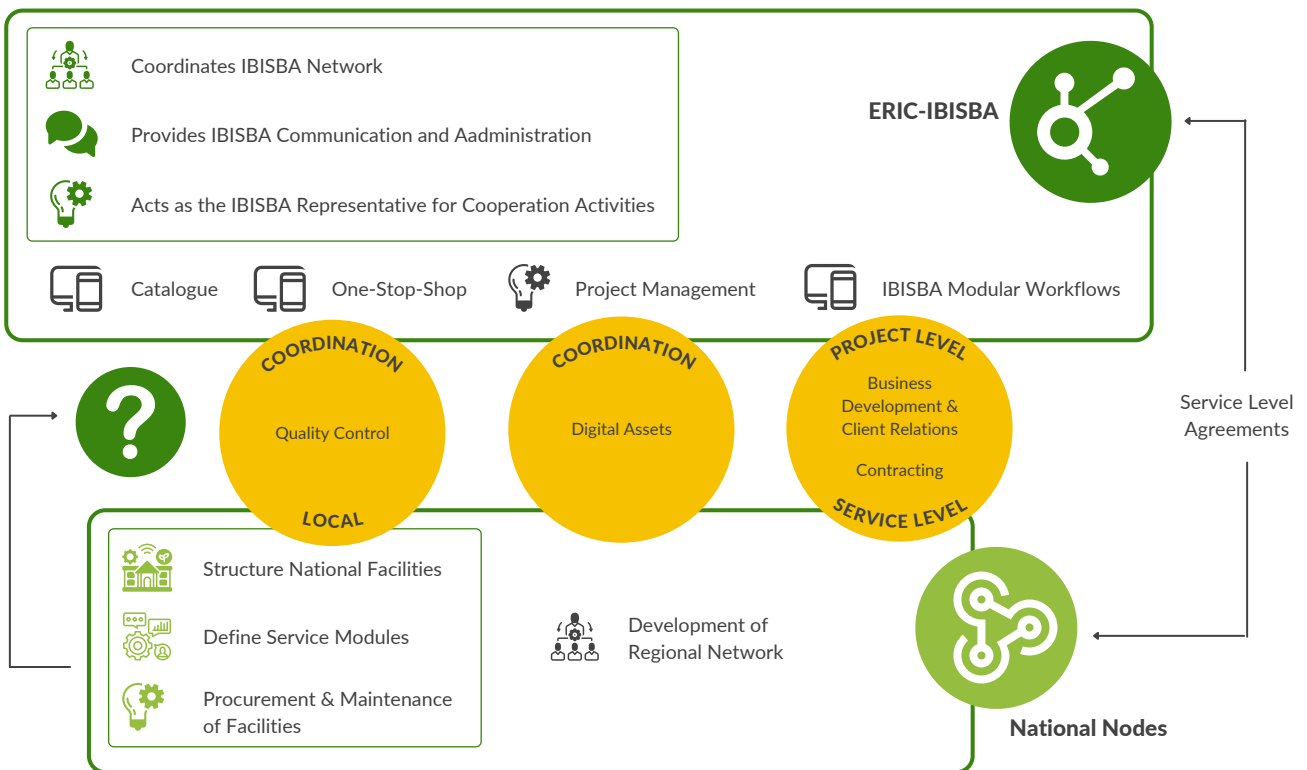
- ERIC-IBISBA includes a **head office** charged with the responsibility to coordinate, communicate, and represent (Figure 12).
- ERIC-IBISBA includes both a **head office and a central management** structure that is fully responsible for the execution of IBISBA business (Figure 13).
- ERIC-IBISBA is both a **head office and a management structure** that is **partly responsible** for the execution of IBISBA business, most sharing this task with National Nodes (Figure 14).



**Figure 12** – The operational perimeter of ERIC-IBISBA is limited to key European level activities. Most functions are produced by the national nodes.



**Figure 13**– The operational perimeter of ERIC-IBISBA englobes most activities. The role of the national nodes is reduced and most competencies are transferred to ERIC-IBISBA.



**Figure 14**– The operational perimeter of ERIC-IBISBA and that of the national nodes is balanced. ERIC-IBISBA adds value to business development and has a mandate to sign off contracts on behalf of some or all facility owners.

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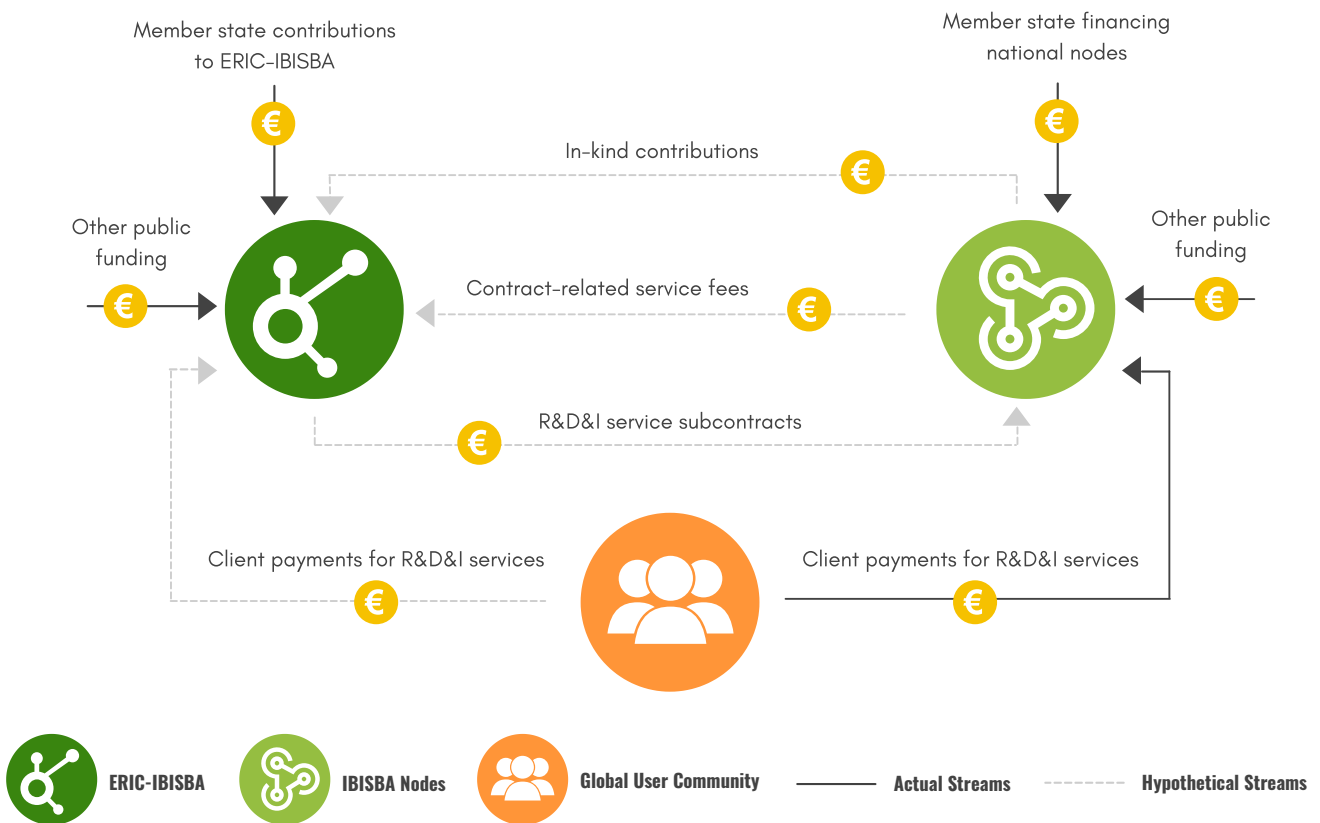
Among these different hypotheses, only the second and third scenarios appear to justify the creation of a legal entity operating under ERIC regime. However, the second scenario is extremely unlikely, because it implies a large transfer of responsibilities from National to European level, leaving national nodes with rather little autonomy. The most plausible scenario is thus the third one, although much work remains to be achieved to allocate the operational functions. **Shared business development** is an interesting proposal, although the relative views of national nodes might be different on this issue. Similarly, considering that the ambition of IBISBA is to seamlessly operate modular project workflows, combining service modules produced by different national nodes, a **single contract framework** is an attractive, but difficult to reach goal for IBISBA. The implementation of such a contracting system would require a **mandate for ERIC-IBISBA to sign off for all facility owners**. It would also imply the creation of a one-size-fits-all contract, where (for example) IPR management policy is fully harmonised. At this stage, it is unclear whether this level of integration can be achieved with all national nodes. It is possible that ERIC-IBISBA would have to establish one type of service level agreement with those national nodes that accept a high degree of integration, while establishing another type of service-level agreement with those nodes that opt out.

### IBISBA's financing framework

At this stage, the financial plan for IBISBA is not yet defined. However, several hypotheses have been identified:

- **Member state contributions** – to ensure the financial viability of ERIC-IBISBA, Member states will be required to pay annual subscription fees, the level of which is fixed through a pluriannual agreement. The basis for the calculation of subscription fees has not yet been examined, but a **fixed fee system** is no doubt the simplest arrangement.
- **ERDF and competitive funding sources** - to enhance the capabilities of IBISBA it is also inevitable that other public funding will be required. At the regional level, it will be important that local authorities continue to provide financial support for facility upgrades, for example earmarking ERDF to support IBISBA. Moreover, at both the national and European levels, IBISBA will need to acquire funding within the framework of competitive project calls.
- **In-kind contributions** – depending on the exact features of ERIC-IBISBA's operational model it is likely that National Nodes will engage in-kind contributions. These can be in the form of financial contributions, for example supporting the financial burden of data storage on a national-based server, and/or staff contributions. Certain ERIC-IBISBA functions can be performed by staff based in national nodes but operating under ERIC-IBISBA management.

- **Service fees** – another hypothesis that could be explored is the principle of service fees. In the event that a strong coordination role is attributed to IBISBA Central, the management component of ERIC-IBISBA, this would involve delivering quite complex services to facilities operating within the IBISBA network. In this case, it is plausible that a part of the operating costs of IBISBA Central could be covered by **service fees**, applied to contracts that are handled by IBISBA central. The exact proposal has not yet been envisaged by IBISBA stakeholders, but this would probably entail the transfer of the extra cost to the client. Nevertheless, the implementation of such a system would only be envisaged if the operating costs of ERIC-IBISBA cannot be met using other funding streams.



**Figure 15 – Financing IBISBA.** The different possible funding streams are identified, although not all are likely to be feasible. In future work, each of these funding streams will be carefully examined. Irrespective of the payment receiver, client payments for R&D&I services will follow a tariffication scheme that differentiates between public and private clients, but also between public sector clients in ERIC-IBISBA member countries and those in other countries.

# Towards ERIC-IBISBA - Next Steps

## Timeline of the Preparatory Phase

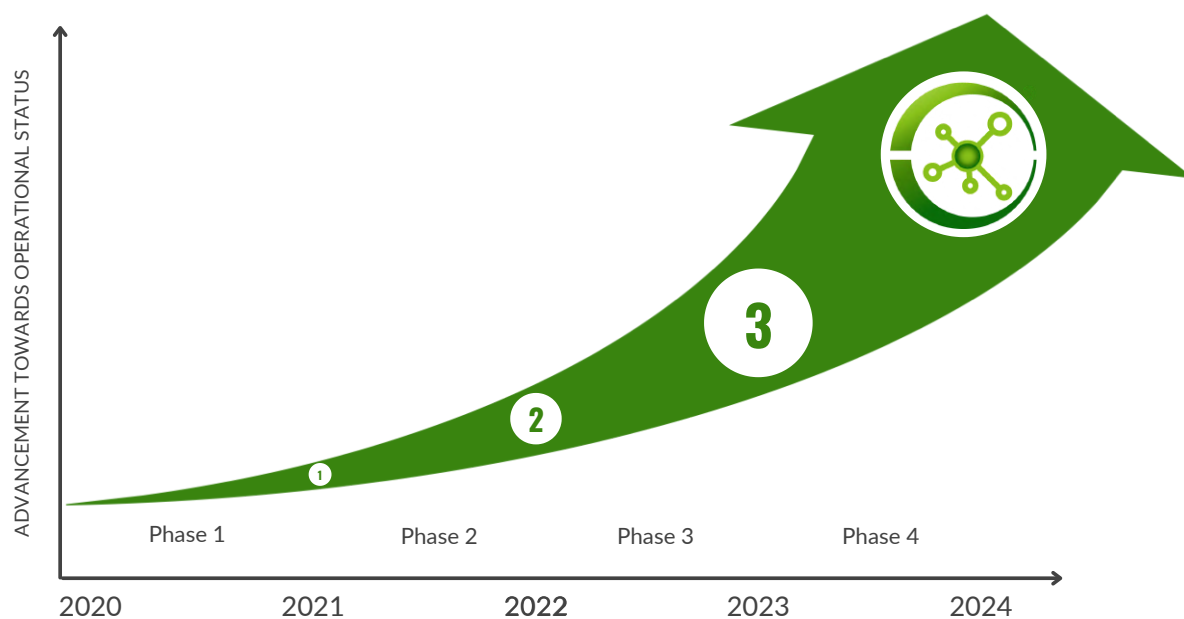
The preparatory phase of IBISBA officially began in January 2020. In the work plan for this important step in IBISBA’s development, 4 phases are planned:

**Phase 1** – Develop and explore the business model and examine possible legal entity options. This phase provides IBISBA stakeholders with information required to make preliminary choices.

**Phase 2** – Stabilize the business model, validate the target legal entity, and develop the financial plan.

**Phase 3** - Finalize the financial plan and prepare the legal statutes of the legal entity. At the end of this phase, the creation of the legal is programmed.

**Phase 4** – Begin pre-implementation of IBISBA as an operational research infrastructure. This phase begins core operations and provides a solid basis to test key business processes.



**Figure 16** – The development of IBISBA its implementation as a legal entity is planned in 4 phases, the target being to establish the legal entity in 2023 or 2024.

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As of June 2021, IBISBA partners have reached a major milestone. Over the initial period of the preparatory phase, considerable effort was focused on the business model and questions regarding the legal entity and its future governance. This has provided a clear indication about how IBISBA will work and has identified an ERIC as the target legal structure.

To create an ERIC, IBISBA stakeholders must now secure support from the founding member countries, working closely with them over the coming phase to build a robust business model and financial plan, acceptable and sufficiently attractive to all parties.

While member countries compose the highest level of governance in an ERIC, research and technology organizations (RTOs) and universities are vital participants in IBISBA, because these own and operate the research facilities that form the IBISBA network and will be primary beneficiaries of IBISBA added value. To better engage with this important stakeholder community, a Memorandum of Understanding has been drafted and is now under appraisal by founding RTOs and universities. **The signature of this MoU** will be an important step in 2021 towards the future pre-implementation of IBISBA.



# Towards ERIC-IBISBA - 1<sup>st</sup> Steering Committee Meeting

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As an early vital step in IBISBA's evolution towards permanent legal status as a European research infrastructure, IBISBA's Steering Committee, composed of Member country representatives, met for the first time on the 17th June 2021 in a remote meeting format. A summary of this meeting is provided below:

## Remote Meeting of IBISBA Steering Committee 17<sup>th</sup> June 2021 | 11:00 - 13:00 C

**Present:** Belgium: Michele Oleo (Flemish department EWI), Finland: Pirjo Kuntinlahti (TEM), France: Eric Guitet and Eric Aubry (MESRI), Greece: Argyro Karachaliou (GSRT), Italy: Grazia Pavoncello (MIUR), Spain: Immaculada Figueroa (Science and innovation Ministry), The Netherlands: Ana de Castro (NWO)

National contacts from IBISBA consortium and national delegates for France, Italy and Spain

**Excused absent:** United Kingdom: Gabriella Pastori, Germany: Andrea Noske

## General Comments

The report (i.e. the confidential version) and the slide deck supplied for the meeting were helpful. These reveal that good progress is being made. It is also encouraging to note that IBISBA is gaining visibility in ESFRI circles, especially among the Life Science Research Infrastructure. The presentation during the meeting answered many questions, although much still remains to be achieved.

In this regard, the Committee expects that future work will focus on refining the business model and on providing additional information regarding the organisation of national nodes and the legal statutes. Moreover, the Committee would appreciate more details regarding IBISBA's timeline and information providing assurance that IBISBA's business model will be model compliant with State aid regulations.

All this information should be compiled and presented at the next Steering Committee meeting.

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## Country-Specific Statements

**Belgium** - political support for IBISBA is based on the fact that IBISBA aligns well with Europe's recovery plan. Nevertheless, if IBISBA wishes to become an ESFRI landmark before renewal of the ESFRI roadmap in 2024, the timeline appears very ambitious. At the regional level, IBISBA is invited to apply for support from the Flemish government.

**Finland** - IBISBA is in line with Finnish expectations. The National Academy of Finland in charge of RI supporting process has already identified IBISBA.

**France** – strong support and principal promoter of IBISBA for its inclusion on ESFRI roadmap. The timeline is ambitious, but feasible. The creation of ERICs is an increasingly a familiar process, so this argues in favour of a shortened timeline.

**Greece** - full political support. Clearly Greek authorities prefer ERIC statutes. Greece is positive about IBISBA and has noted that there is some new traction at the national level with requests to compose the national node coming from the Food innovation research infrastructure and from the Athena Research Centre. This is positive.

**Italy** - IBISBA was recently included on the Italian research infrastructure roadmap and benefits from national financial support (€200k in 2021).

**Spain** - IBISBA benefits from political support in Spain. Significant work remains to be achieved by the IBISBA partners in Spain to mobilise other Spanish partners to complete the Spanish node. It will be important to assess the added value for Spain and estimate the return on investment.

**The Netherlands** - Wageningen University is on the infrastructure roadmap and there is a good level of liaison with IBISBA. The Ministry is monitoring progress and note that the timeline is very ambitious.

**United Kingdom and Germany** - both countries are interested in IBISBA and will be monitoring future developments.

