PATHFINDER CHALLENGE
Engineered Living Materials (ELMs)
CHALLENGE GUIDE – PART I

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Challenge page: https://eic.ec.europa.eu/calls-proposals/eic-pathfinder-challenge-engineered-living-materials_en

CONTENT

The Appendices that are referred to in this document are common to the different Challenges and bundled in Part II of the Challenge Guide, published on the Challenge page on the EIC Website https://eic.ec.europa.eu/calls-proposals/eic-pathfinder-challenge-engineered-living-materials_en.

1. About this document

The Challenge Guide is the reference document accompanying a Pathfinder challenge along its whole life cycle, from call to achieving its objectives.

The Programme Manager in charge of this Pathfinder Challenge is the editor of the Challenge Guide. The Challenge Guide captures, at any moment, the state of play, achievements and remaining challenges, and documents the process by which the Programme Manager and Portfolio members jointly establish an evolving set of Portfolio objectives and a shared roadmap for achieving them. The most recent version can be found through the corresponding Challenge page on the EIC Website https://eic.ec.europa.eu/calls-proposals/eic-pathfinder-challenge-engineered-living-materials_en.

The Challenge Guide starts out as a background document to the initial Pathfinder Challenge call. It details the intention of the call by complementing notably the scope, objectives (see Section 5 - Challenge call text) or criteria (see Appendix 3: EIC 2021 Work Programme – Evaluation criteria) set out in the EIC Work Programme. In no case does it contradict or supplant the Work Programme text. After the call evaluation, the Challenge Guide further documents the initial Challenge Portfolio that resulted from the call.

As the actions in the Portfolio unfold, the Challenge Guide further documents the evolving Portfolio Objective(s) and the progress towards achieving them, notably through the Portfolio Activities that the Programme Manager puts in place.

The Challenge Guide serves as a reference for the common understanding, rules-of-play and obligations for the EIC beneficiaries that are involved in the Challenge Portfolio. Contractual Obligations are further reference material from the EIC Work Programme are collected in Part II of the Pathfinder Challenge Guide, published on the Challenge page on the EIC Website https://eic.ec.europa.eu/calls-proposals/eic-pathfinder-challenge-engineered-living-materials_en.

2. Overall objective of the Pathfinder Challenge

This section sets out the rationale of the Challenge. Building on the state of the art in the relevant scientific and technological domains, it motivates the challenge, sets the boundaries of its scope and explains the overall objectives. This section should be read as further background to the Challenge specific part of the EIC Work Programme text (see Appendix 2).
Proposals to this Challenge are expected to explain how they relate to and intend to go beyond the state of the art, and how they interpret and contribute to the objectives of the Challenge.

2.1 Background on ELMs

The unmatchable properties of materials in nature have been long recognised. For millennia, these materials have been exploited for multiple purposes. In this century, they provided inspirations for artificial materials with unique properties (biomimetic materials). In addition, the biosynthetic pathways of nature biopolymers and their chasses have been hijacked for making biobased materials with unique renewable, recyclable and biodegradable potentials. More recently, the combination of artificial and biological components in a material (biohybrid material) has allowed to expand even further the range of functionalities[1]. These recent advances have established a market and stimulated demand for nature's or nature-like materials thanks to their new performances and (oftentimes) reduced environmental impact compared to traditional human-made materials. However, despite their significant contributions, these materials have also limitations compared to materials in nature in the degree to which they are environmentally friendly and energy-efficient, and in the range of their properties. These limitations are mainly due to the fact that all these materials are not living and as such they do not have all the hallmarks of a living material from nature to self-heal or -regenerate, adapt to environmental clues, be long lasting and sustainable. What if materials with these characteristics could be made? Which kind of new applications will be possible?

The emerging field of Engineered Living Materials (ELMs) has recently shown that these materials can be made. **ELMs are defined as materials composed, either entirely or partly, of living cells[23], thus displaying the unique combination of properties of self-healing or regeneration, adaptation, longevity and sustainability**. ELMs are classified in two groups[4]. Biological ELMs[3] are entirely self-assembled by living cells via a bottom-up process and composed by cells and their products. They may also contain an inorganic component, but

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[1] Most biohybrid materials are not living with exceptions of few in which the biological component is living cells. However, even these biohybrid materials are de-facto abiotic as the cellular component does neither actively generate nor modify the properties of the bulk material [Nguyen *et al.* (2018) DOI: 10.1002/adma.201704847].
[2] Nguyen *et al.* (2018) Engineered Living Materials: Prospects and Challenges for Using Biological Synthesis to Direct Assembly of Smart Materials. *Advanced Materials 30 (19):* e1704847. DOI: 10.1002/adma.201704847
[3] Glbert, C.and Ellis, T. (2019) Biological Engineering Living Materials: Growing Functional Materials with Genetically Programmable Properties *ACS Synthetic biology 8:* 1-15. DOI: 10.1021/acssynbio.8b00423
[4] Srubar III, Wil V. (2020) Engineered Living Materials: Taxonomy and Emerging Trends. *Trends in Biotechnology*, corrected proof. DOI: 10.1016/j.tibtech.2020.10.009

only if its presence is due to biological processes e.g. via biomineralisation[3]. Hybrid living materials (HLMs[5,6]) are only partly self-assembled and composed by living cells (and their products). They are built via a top-down process, e.g. casting or embedding in artificial matrices, and bioprinting[2,4]. Direct modification of the abiotic component by the cells or by dynamic interactions between the cellular and abiotic components endows a HLM with its properties.

In all ELMs, the cellular component extracts energy from the environment to form or assemble entirely or partly the material itself, to adapt its morphology and to respond to environmental stimuli[7]. In other words, ELMs are materials made close to their final forms via self-assembly and self-functionalisation of the cellular component and, thus, potentially requiring a significantly simplified manufacturing process compared to other advanced materials. This simplification is illustrated by the recent factory-scale, cost-competitiveness and environmentally friendly *in situ* production of mycelium-grown materials for packaging and constructions, which have been successfully commercialised[2,8]. However, since the mycelia are killed during production, these products do not retain the full benefits of ELMs. By being alive, ELMs represent a fundamental change in materials' production and performance, enabling new, similar or better functionalities, compared to traditional materials but with decreased costs, and environmental impact[2-4].

Many different factors have contributed to the current emergence of ELMs such as an ever-growing understanding in microbial and human cellular functions, in biopolymer biosynthesis and self-assembly, in natural morphogenic processes (incl. stem cells morphogenesis), coupled with recent technological advances in synthetic biology, additive manufacturing, and control engineering. Some examples of proof of concepts of applications of ELMs enabled by these advances are[2-4]: 1) biocement made under mild conditions by photosynthetic bacteria to create bricks able to exponentially regenerate and to be entirely recyclable, 2) long-lasting hydrogel materials with bacterial spores, which once germinated, sense and kill pathogens, 3) a material able to form *in situ* to protect and regenerate gut lining against Inflammatory Bowl Disease, and 4) a programmable biofilm matrix whose formation is triggered under specific concentration of mercury and, once it is formed, it sequesters mercury. These and other examples[2-4,9] show the potential for example for living building materials, therapeutics, electronics, devices, soft robotics and composite[3,10].

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[5] Tang *et al.* (2020) Materials design by synthetic biology. *Nature Reviews Materials*. DOI: 10.1038/s41578-020-00265-w;

[6] Soo Hoo Smith *et al.* (2019) Hybrid Living Materials: Digital Design and Fabrication of 3D Multimaterial Structures with Programmable Biohybrid Surfaces *Advanced Functional Materials*. DOI: 10.1002/adfm.201907401; https://www.media.mit.edu/projects/hybrid-living-materials/overview

[7] Text in italics is verbatim from the ELMs Challenge text call of the EIC 2021 WP.

[8] https://ecovativedesign.com/

[9] Appiah *et al.* (2019) Living Materials Herald a New Era in Soft Robotics. *Advanced Materials 31*. DOI: 10.1002/adma.201807747

[10] Davies *et al.* (2020) Engineering Pattern Formation and Morphogenesis. *Biochemical Society Transactions 48*: 1177-1185. DOI: 10.1042/BST20200013

2.2 Challenges in ELMs

While promising for the future, all the currently produced ELMs are no match to nature's materials in terms of:

1) Complex function. Despite the big variety of microorganisms producing extracellular polymeric materials, current ELMs have been limited to a handful of very common microorganisms chosen for their genetic tractability and/or specific properties (e.g. *E.coli*, *Bacillus*, *Pseudomonas, Shewanella*, *Saccharomyces* and few others)[2-4]. Plants and mammalian cells have been tested to an even much lesser extent. Almost all ELMs are made from a single chassis and very few are from engineered consortia[11]. All this has contributed to the limited functionalities of ELMs, even if the use of programmable cells has been instrumental in broadening the range.

2) Size/scale-up. The size of the ELMs so far achieved has been limited from nano to milli scale for bottom-up reaching in few cases the cm scales, and in the cm scales for top-down approaches with few ad hoc examples close to the meter scale. Size control in all scales and scale-up is difficult due to a lack of spatio-temporal control of cell growth and cellular viability. Some progress in issues of scale has been achieved in HLMs by the adoption of additive manufacturing but even here scaling-up in size is hampered e.g. by cell viability. Scale-up issues are not just across size but also in production rates and volumes.
3) Complex structure. The lack of spatio-temporal control of material growth across scales has not only contributed to limiting the size of ELMs but also to their spatial heterogeneity and structural complexity. Albeit pattern formation has been reported in biological ELMs and HLMs[3], it is mostly limited to one pattern at nano- and micro-level. 3D heterogeneity and complex architecture are yet to be achieved. An interesting new technology, Menifluidics[12], shows some promise as it is able for the first time to control spatio-temporally the growth of microbial colonies. Pattern formation of mammalian cells has been reported in only very few cases and in multicellular structures at the milliscale[3]. Despite the challenges, controlled mammalian pattern and 3D structure formation is of high interest for its potential leading to the creation of tissues and organs[3,8] via synthetic and programmable morphogenesis.

4) Long-term viability, genetic stability and robustness. Long-term cell viability under non-*in vivo* conditions is a general challenge in ELMs, especially in HLMs. Advances in top-down approaches have been made for short-term viability by using hydrogel containing cells or spores with survival of several days up to few weeks. The use of spores has also enabled short-term cell survival under harsh chemical and physical conditions[2-4]. For cells to remain viable not only they need to survive but they need to be genetically

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[11] Gilbert *et al.* (2021) Living Materials with Programmable Functionalities Grown from Engineered Microbial Co-cultures. *Nature Materials.* DOI: 10.1038/s41563-020-00857-5

[12] Kantsler *et al.* (2020) Pattern Engineering of Living Bacterial Colonies Using Meniscus-Drive Fluidic Channels. *ACS Synthetic Biology 9*: 1277-1283. DOI: 10.1021/acssynbio.0c0014

stable. ELMs are in such an early stage of development that genetic stability and system robustness (i.e. the ability of ELMs to perform their function safely and reliably under stress and/or in the long-term) have not yet been tested systematically. However, these issues need to be tackled if ELMs development were to advance. Nature has clearly found a solution to maintain the stability of nature's materials even if they are formed by cells with a tendency to evolve. Control of genetic stability (especially key in engineered cells) is also required to prevent genetic transfer in the surrounding ecosystem within the material and outside.

These current shortcomings of ELMs are interdependent and they all derive from the inability to control spatio-temporally the simultaneous processes of material self-assembly and genetic functional programming. This is mainly due by the lack of closed-loop systems for the production of ELMs. The progress achieved so far in ELMs has been via open-loop systems requiring a lot of intensive and time-consuming manual processing steps. These systems lack the ability to be generalizable and scalable, and to produce predictable and reproducible ELMs. A noticeable exception is the recent HLM automatized fabrication platform showing an unprecedented controlled production of a HLM[6]. **The major technical challenge in ELMs is to achieve an automated closed-loop spatio-temporal control for the production of a wide range of ELMs materials with precise, predictable and complex 3D architectures and functions across multiple scales.** Intrinsic to this challenge is a need of new capabilities in robust design principles and platform technologies in computation (incl. ML and AI), synthetic biology and manufacturing to:

- control precisely cell morphogenesis, self-assembly and cellular-abiotic assembly of materials from micro to macro scale incl. the interplay between cellular and abiotic component;
- account and control for cell variability and external factors thus improving robustness, reproducibility, stability and performance of the materials;
- create materials with multi-cellular consortia across multiple scales with spatio-temporal controlled cell-cell communication leading to tuneable and autonomous patterning enabling different 3D architecture, material properties and functions within the same material;
- self-contain and control the life-span of the genetically modified cells used in ELMs (e.g. for those applications that entail release in the environmental) to address concerns of safety and biocontainment;
- be able to adapt platform technologies for the reliable customisation of ELMs, i.e. for a wide variety of ELMs in terms of size, shape, cellular composition, properties and functions.

The ELMs field is in its infancy and significant technological development is needed before the field matures from research to commercialisation. Nonetheless, the ELMs technological development needs to be socially responsible by taking into account possible future societal, ethical, economic and environmental impacts, which might block the path to the market.

Safety concerns and regulatory hurdles need to be addressed early on to enable such a shift. Similarly, a lesson from the standardisation activities in synthetic biology clearly points out that it is never too early to include assessment of standardisation needs and development. Calls for standardisation in ELMs have been raised in recent reviews[4,5]. Assessment of needs and eventual development of standardisation will need to go hand in hand with ELMs technology development to boost ELMs research and innovation by enabling the comparison, codification and interoperability of results and technologies; for accountability and conformity to regulations; and for scaling-up manufacturing procedures and the quality assessment of products; and for commercialisation. Challenges are in the paucity of existing standards in synthetic biology and by the new "product" concept of a material alive. The concept of a material alive with engineered cells could slow down societal (and consumers') acceptance of ELMs, thus requiring an early engagement in a social dialogue with the public at large, but also with potential consumers and with representatives from the relevant materials' sectors to be penetrated by ELMs.

2.3 Rationale for the ELMs Challenge[13]

ELMs can possibly transform virtually every modern endeavour from healthcare to construction and everything in between. The emergent nature of the field and its broad potential in many economic sectors present a unique opportunity to catalyse a strong innovation community in Europe accelerating the creation of a new market in ELMs. Despite accounting for the emergent and very small size of the ELMs field, an analysis of publications in ELMs and EU funding[14] shows Europe somewhat lagging behind. Nonetheless, few small companies worldwide, of which two in Europe, focus on ELMs (albeit mostly with non-engineered cells) or materials similar to ELMs (such as the mycelium mycelium-based products already mentioned in which the living component is killed in production). This promising signal and the very early stage of the field leaves plenty of room for a nascent European ELMs community to flourish.

2.4 ELMs Projects

This ELMs Projects section refers only to ELMs projects funded under the ELMs call and not to projects on ELMs funded by the EIC Open calls. This section 2.4 shall be read with sections 2.1, reporting the definition of ELMs for the purpose of the call (also in the EIC 2021 WP ELMs call) and the state of the art, and 2.2, describing the challenges in the field and combined they shall help applicants to develop proposals responsive to the call.

2.4.1 Objectives of the ELMs Call

The specific objectives of the ELMs call as described in the EIC 2021 WP are:

[13] Hereafter "Portfolio" refers to the "ELMs Portfolio"; "beneficiaries" refers to "the beneficiaries of the Pathfinder ELMs Challenge"; and "ELMs call" refers to the "Pathfinder Challenge ELMs call".

[14] To the best of our knowledge and analysis of ERC, FET Open, FET Proactive, EIC Pilot Pathfinder and Accelerator projects. To the best of our knowledge, this is also the first top-down call of the European Commission on ELMs.

- to support the development of new technologies and platforms enabling the controlled production of made-on-demand living materials with multiple predictable dynamic functionalities, shapes and scales;
- and to build a community of researchers and innovators in ELMs through portfolio's activities.

Reaching these objectives requires a research team that strongly integrates, among others and not exclusively, expertise in synthetic biology, materials engineering, control engineering, additive manufacturing, artificial intelligence, synthetic or engineered morphogenesis as well as ethical, legal and social aspects (ELSA).Collaborations with researchers outside the MS and Associated countries is welcome.

2.4.2 Specific Conditions

In order to apply, as per the ELMs call proposals must:

- plan to validate the technologies by producing at least two different living materials (i.e. with different applications, scale - 10 x difference- and cellular composition). These must not be a derivative of each other. Please notice that "different applications" means applications in different sectors thus one can be in health and the other in environment;
- the material needs to be formed by living cells as per the definition of ELMs in the introduction of ELMs call. Alternatively if a synthetic cell is used, the synthetic cell must have, prior to the start of the project, a demonstrated ability (via a peer-reviewed scientific publication) of cellular reproduction via cell division and adaptation to environmental clues;
- define an integrative approach to assess the needs and implications of the technologies and their limits, including ethical and regulatory requirements.

2.4.3 Expectations from Projects Funded under the ELMs Call

The specific expected outcomes depending on the choice of the ELM production process (top-down or bottom-up) as per the ELMs call are:

- a proof of principle of technologies far beyond the current state of the art enabling the production of a minimum of two novel biological ELMs, bigger than 1 cm in all dimensions for one of the materials, by programmable and controlled synthetic or engineered morphogenesis (whether with eukaryotic or prokaryotic cells);

or

- a laboratory validated, automatized and computer-aided design-build-test-learn (DBTL) platform far beyond the current state of the art able to produce a minimum of two novel HLMs in multiple scales with enhanced or unprecedented properties.

As stated in section 2.2, the major technical challenge in ELMs is to achieve an automated closed-loop spatio-temporal control for the production of a wide range of ELMs materials with precise, predictable and complex 3D architectures and functions across multiple scales.

In order to overcome this challenge and reach the objectives of the ELMs call, projects funded by the ELMs call are strongly encouraged to address the main ELMs challenge and the specific ones described in section 2.2. In addition, projects are strongly encouraged to:

- have a duration of 5 years considering the objectives of the ELMs call and Portfolio;
- plan the finalisation of the technical tasks by month 58 to leverage the final technical outcomes for exploitation and dissemination activities of the project and the Portfolio;
- report at the proposal stage relevant metrics, and set mid-term and final quantitative milestones for each technical task to address how the technical progress is measured and demonstrated;
- take into consideration the Portfolio roadmap in the project implementation plan;
- demonstrate at the proposal stage the innovation potential beyond the current state of the art of the platform technologies proposed by identifying appropriate performance metrics and qualitative properties for each technology;
- identify at the proposal stage metrics to define the performance and characteristics of the final ELMs to be produced; among others, these metrics shall reflect diversity in structure, cellular components, functions, size, and long-term viability, and, whenever applicable, they shall be compared with current state of the art;
- address the potential integration of technologies and relevant specifications;
- address the safe and responsible development of the proposed technologies and ELMs materials at the proposal stage;
- address IPR strategy for each potential innovation and clearly report the strategy for each identified potential innovation at the proposal stage;
- address the dissemination and communication activities at the proposal stage by clearly identifying the type of event, the audience size, the audience target and the main message.

As per the ELMs call, projects are also strongly encouraged to:

- consider the production of multi-cellular ELMs;
- develop technologies that can be easily generalizable and adapted for the production of a broad range of ELMs from different cells;
- (specifically for biological ELMs) develop laboratory validated automatized and computer-aided design-build-test-learn (DBTL) platform (for HLMs projects this is a requirement);
- (specifically for HLMs) consider using different abiotic components in the two HLMs materials.

3. Proactive Portfolio Management

Proactive portfolio management represents, for the EIC Pathfinder, a novel practice that underlines not only the ambition to fund high-risk projects, but also the imperative to change *from a grant-giving agency (the dominant paradigm throughout Europe) to a hands-on innovation agency for all funded projects.*

This section describes the EIC proactive management as applied to the Pathfinder Challenge. It starts by building the portfolios; i.e. by allocating actions into portfolios (3.1). Proactive management will allow to define and to update portfolio's objective and roadmap (3.2). Portfolio members will benefit from portfolio activities and from the access to the EIC Market Place (3.3).

3.1 Portfolio-based Considerations for the Selection of Proposals for Funding

This section provides the Challenge specific elements of the way in which the evaluation results in a coherent Challenge Portfolio. It should be read in conjunction with the overall evaluation process as described in the EIC Work Programme text (Appendix 3).This section provides guidance to applicants on how to align their proposal with the architecture of the Challenge Portfolio as envisaged by the Programme Manager.

At the second evaluation step, the evaluation committee, chaired by the Programme Manager, builds a consistent Challenge portfolio, i.e. a set of actions supported by the EIC under Pathfinder. In order to do so, the evaluation committee will allocate proposals into categories. These categories define the overall architecture of the targeted portfolio.

Before applying the categorization and the general considerations described here below each proposal will have to satisfy the definition of ELMs, the specific conditions and specific expected outcomes described in sections 2.1, 2.4.2 and 2.4.3, respectively. For this specific Challenge, the evaluation committee will then consider the following categories:

- HLMs
- Biological ELMs

A proposal may be allocated to both of these categories if they satisfy the specific expected outcomes for each category described in section 2.4.3. In this case the evaluation committee will have to evaluate the proposal based on all the considerations listed here below i.e. those applicable to both categories and those specific to the HLMs and the biological ELMs.

Within each of these ELMs categories (i.e. HLMs or biological ELMs), the evaluation committee will look for a **diverse portfolio of platform technologies under closed-loop control with high accuracy in reproducing and predicting ELMs characteristics, and with claims based on specified metrics and on specific test-beds**, using the following **general considerations**:

a) proposals with some programmable cells; among these preference to proposals with multi-cellular ELMs if they are aligned with consideration a); in the event of comparison of proposals with unicellular ELMs diversification of the cellular components in the Portfolio (incl. accounting for the multicellular proposals) may be taken into account;

b) diversity in the technological approaches proposed and generalizability of such technologies;
c) diversity in material properties and functions.

Within the **HLMs category** in addition to the general considerations a)-c) mentioned above, the evaluation committee will also **specifically considered** the diversity of the abiotic components.

Within the **biological ELMs category** in addition to the general considerations a)-c) mentioned above, the evaluation committee will also use the following **specific considerations**:

d) a balance or close to a balance shall be reached between proposals with mammalian cells and those without but only if it is aligned a);
e) proposals with automatized and integrated platform technologies.

After evaluating the proposals within each category, the evaluation committee shall make a final selection of the proposals from both categories so that a **balance or close to a balance between proposals on biological ELMs and those on HLMs** is reached. The type of applications will not be a portfolio consideration due to the intrinsic diversity present in each proposal as a consequence of the ELMs call's requirement of at least two ELMs with different applications (where by "different applications" is meant applications in different sectors e.g. one in health and the other in environment).

The selected actions, once funded, will be included in the EIC Challenge Portfolio. The contractual obligations subsequent to the participation of an action into a Challenge portfolio are described in Appendix 1.

3.2 Portfolio Objectives and Roadmap

The ELMs call and the Portfolio associated with it aim to seize the opportunity to position Europe strategically at the forefront of the ELMs field and to overcome the technological challenges to harness the engineering potential of nature for the production of living materials. Initially, projects funded by the ELMs call will mainly compose the Portfolio with the two identified Pathfinder Open projects in this area. The Portfolio size might increase with the addition of relevant projects funded through future EIC Open calls. ELMs projects funded from the EIC Open calls will contribute to the Portfolio activities as described in the EIC 2021 WP. However, the achievement of the proposed objectives of the Portfolio shown below, which are dependent on the objectives of the ELMs call (see section below on the ELMs Projects), hinges mainly on the proactive participation in Portfolio activities by projects funded under the ELMs call. The proposed specific objectives of the Portfolio are to:

- contribute to catalyse and facilitate the advancement of ELMs scientific and technological development and its translation across Europe, and at the same time position the ELMs European community on the international stage by disseminating and exchanging knowledge and approaches both within and outside the Portfolio[15], and building relationship with partners that will benefit the field as a whole;

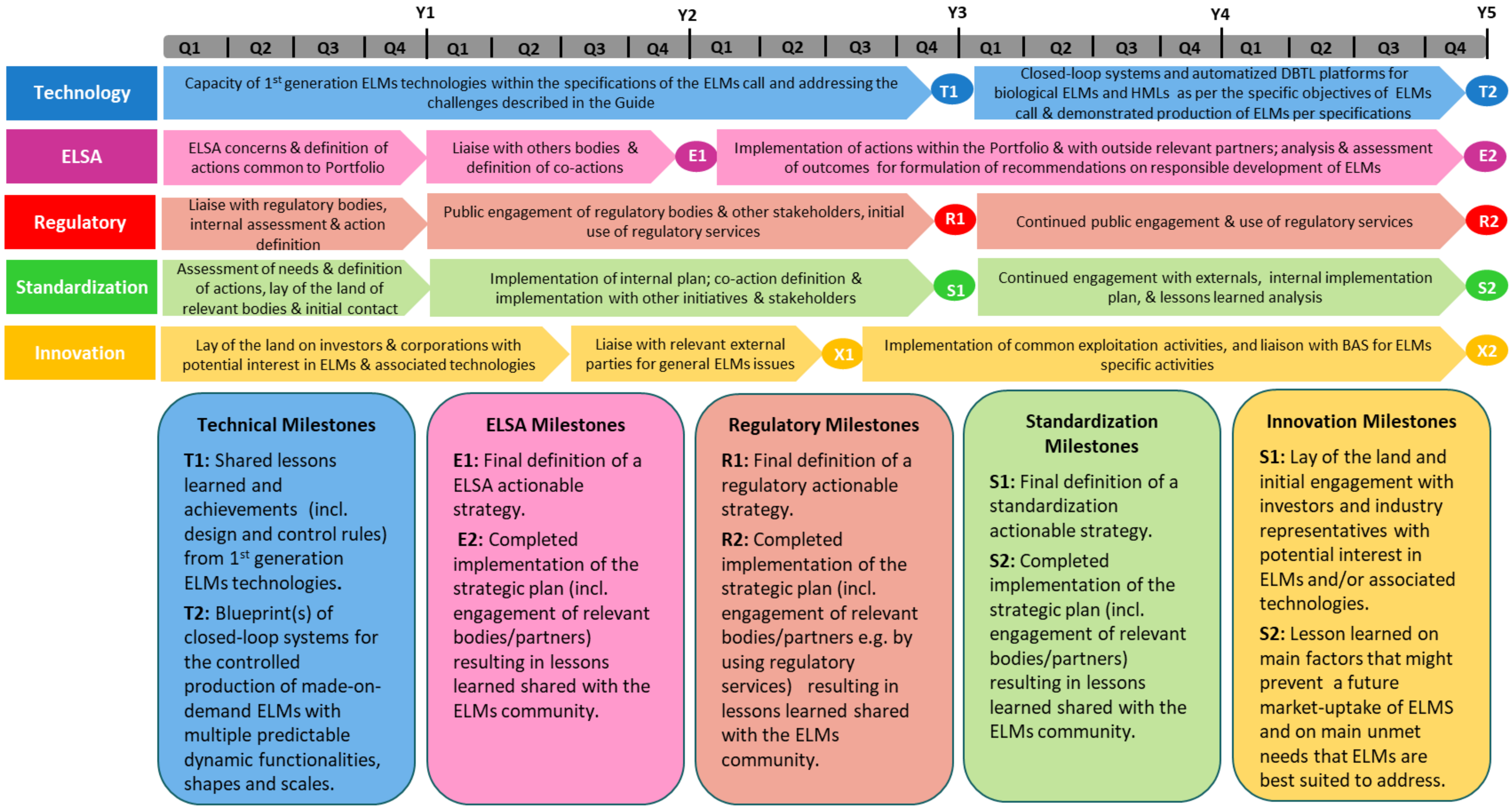
- assess and address the ELMs portfolio needs, and collaborate and contribute to the regulatory debate by engaging early on and continuously with regulatory bodies;
- anticipate and address ethical, legal and social aspects (ELSA) issues by engaging early on and continuously with policy makers and the public at large as well as building relationship with relevant partners with whom to join forces, and by sharing also best practices and guidelines when applicable (e.g. biosecurity and biosafety); responsible research and innovation methods should guide the research and technology development in the Portfolio;
- assess and address the ELMs portfolio needs in standardisation, and collaborate and contribute to the ELMs standardisation development and debate by building relationship with relevant partners with whom to join forces;
- identify common barriers specific to the adoption of the ELMs innovation and to future ELMs commercialisation such as elements discouraging investor buy-in and customer adoption, and engage early on with relative stakeholders as well as leverage or co-organise related activities with the EIC Business Acceleration Services.

The proposed roadmap with relevant milestones and tasks proposed for the Portfolio is shown in Figure 1. These initially proposed objectives and roadmap with relevant milestones and tasks are not intended to limit additional ideas from applicants responding to the ELMs call. On the contrary, **applicants are strongly encouraged to propose any additional objectives and milestones for the Portfolio**. **The portfolio activities shall be described in a dedicated work package with an allocated budget**. The PM's initial proposal of the objectives and roadmap for the Portfolio described in this section and the proposals of the projects to be funded under the ELMs call will be taken into account to finalize the objectives and roadmap with associated milestones, tasks and deliverables of the Portfolio. This will be done via consultation with the beneficiaries during the Grant Agreement preparation phase. The work package of Portfolio activities of each project will be revised based on the jointly agreed Portfolio activities before the grant agreement signature. It is this revised version that will be implemented to achieve the Portfolio objectives.

As the projects and the field progress, the roadmap and associated milestones and deliverables can be further reassessed during the life-time of the Portfolio by the PM following consultation with the beneficiaries and, where appropriate, with other interested members of the EIC Community and other third parties. It is important to note that, while there could be synergies between a Portfolio and a project's activity, the Portfolio activities are no substitute to the project's activities and requirements (e.g. in exploitation, dissemination and communication specific to the project).

[15] In accordance with section 4 and 5 of Annex 7 of the WP.

Figure 1: Roadmap with relevant milestones and tasks proposed for the Portfolio



3.3 Portfolio Activities and EIC Market Place

The roadmap proposed in section 3.2 provides examples of portfolio activities. As mentioned in Section 3.2, the proposed portfolio objectives, roadmap and activities will be further modified during the Grant Agreement preparation phase by taking into account what the projects have proposed as well. A consultation between the Programme Manager and the projects at this stage will lead to the finalization of the Portfolio activities to be included in the grant agreement as already described in section 3.2.

As also mentioned in section 3.2, the achievement of the objectives and the implementation of the roadmap of the Portfolio hinges mainly on the proactive participation in Portfolio activities by projects funded under the ELMs call. Therefore, the beneficiaries are expected to work in close collaboration and in a proactive manner. To this end, in the first two months of the life-time of the projects the PM will work cooperatively with the beneficiaries to define the governance structure of the Portfolio[16], to establish expectations of the projects working together, to define rules for resource and data sharing within the Portfolio in accordance to Annex 7 of the EIC 2021 WP, and identify the communication and dissemination strategies for the Portfolio. All these elements will be further finalised during the Portfolio kick-off meeting and written in the Portfolio Implementation Strategic Plan. Thus, projects are strongly encouraged to have the following common activities and associated deliverables for the coordination of the Portfolio activities:

- ELMs Network kick-off meeting and its report by month 3;
- an ELMs Network web page with link to all the projects part of the Portfolio and report by month 3;
- Portfolio Implementation Strategic Plan by month 4;
- ELMs Network annual meetings (with a minimum of two in-person meetings) and its report one month after the annual meeting.

As mentioned in **Section 3.2**, the projects are strongly encouraged to **include a work package specific for portfolio objectives and activities and to allocate a budget for these activities**. To ensure a proper coordination of the Portfolio activities a **common start date** for all projects funded by the ELMs call will be selected during the Grant Agreement preparation in consultation with all the beneficiaries.

To facilitate the exchange of information and data, to enhance cross-fertilization activities, and to stimulate and nurture potential innovation, the EIC Programme Manager may request any beneficiary to make available - through the EIC Market Place - information on preliminary findings and results generated by the action, with the aim to probe their potential for further innovation.

[16] For any activities with external partners and for communication and dissemination, the Portfolio will be named ELMs Network.

The EIC Market Place will support the proactive management of the portfolio by allowing the Programme Manager to have an overview of the actions, their preliminary findings and potential links between those, thanks to the underlying Artificial Intelligence tool.

The Programme Manager will accelerate the most promising portfolio projects based on work progress against previously set milestones and using the power of innovation intelligence. To accomplish that, the Programme Manager disposes of EIC tools such as, fast tracking a project to Accelerator (see Appendix 2, Active management section) and a 50K grant that can be used more than once, to the benefit of a beneficiary (See Appendix 4). Regarding the latter, the beneficiary must provide to the Programme Manager convincing and fully documented evidence that the project has arrived at a new, rather unexpected outcome that opens new opportunities and, therefore, new or additional market search and business intelligence analysis are needed.

4. List of Projects in the Pathfinder Portfolio ELMs

(will be completed after the evaluation of the Call and updated with any other projects, e.g., from Pathfinder Open, joining the portfolio)

5. Challenge call text

(extract from https://eic.ec.europa.eu/system/files/2021-03/EIC%20Work%20Programme%202021.pdf)

Engineered living materials (ELMs) are composed, either entirely or partly, of living cells. ELMs entirely composed of living cells are called biological ELMs and they self-assemble via a bottom-up process –e.g. synthetic morphogenesis for organoids' production. ELMs only partly composed of living cells are called hybrid living materials (HLMs) and are built with a top-down process with integrated polymers or scaffolds. In both cases, the cellular components extract energy from the environment to form or assemble the material itself, and to adapt its morphology and function to environmental stimuli. This endows these materials with a combination of properties not present in any non-living material: self-regeneration, adaptation to environmental clues, longevity and environmental sustainability. By being alive, ELMs represent a fundamental change in materials' production and performance, enabling new, better or similar functionalities, compared to traditional materials but with decreased costs and environmental impact. ELMs have the potential to transform virtually every modern endeavour from healthcare to infrastructures to transportation.

With this Pathfinder ELMs Challenge, the EIC seeks to seize the opportunity to position strategically Europe at the forefront of the ELMs field, which is still in its infancy. This Pathfinder Challenge aims to overcome the technological challenges to harness the engineering potential of nature for materials' production. The specific objectives of this call are to support the development of new technologies and platforms enabling the controlled production of made-on-demand living materials with multiple predictable dynamic functionalities, shapes and scales; and to build a community of researchers and innovators in ELMs. Reaching these objectives requires a research team that strongly integrates, among others and not exclusively, expertise in synthetic biology, materials engineering, control engineering, artificial intelligence, synthetic or engineered morphogenesis as well as ethical, legal and social aspects (ELSA).

Projects under this call are expected to develop technologies for the production of a minimum of two different living materials (i.e. with different applications, scale -10 x difference-and cellular composition). The specific expected outcomes depending on the choice of the ELM production process (top-down or bottom-up) are:

- a proof of principle of technologies far beyond the current state-of-the-art enabling the production of a minimum of two novel biological ELMs bigger than 1 cm in all dimensions by programmable and controlled synthetic or engineered morphogenesis (whether with eukaryotic or prokaryotic cells);

or

- a laboratory validated, automated and computer-aided design-build-test-learn (DBTL) platform far beyond the current state-of-the-art able to produce a minimum of two novel HLMs in multiple scales with enhanced or unprecedented properties.

Projects are strongly encouraged to consider multi-cellular ELMs. They are also encouraged to develop technologies that can be easily generalizable and adapted for the production of a broad range of ELMs from different cells.

Projects funded under this call are also expected to collaborate and contribute to the wider ethical, societal and regulatory debate.

Specific conditions for this challenge

In order to apply, your proposal must plan to validate the technologies by producing at least two different living materials (i.e. with different applications, scale -10 x difference-and cellular composition). These must not be a derivative of each other. The material needs to be formed by living cells as per the definition of ELMs in the introduction of this call. Alternatively, if a synthetic cell is used, the synthetic cell must have, prior to the start of the project, a demonstrated ability (via a peer-reviewed scientific publication) of cellular reproduction via cell division and adaptation to environmental clues.

Your proposal also needs to define an integrative approach to assess the needs and implications of the technologies and their limits, including ethical and regulatory requirements.