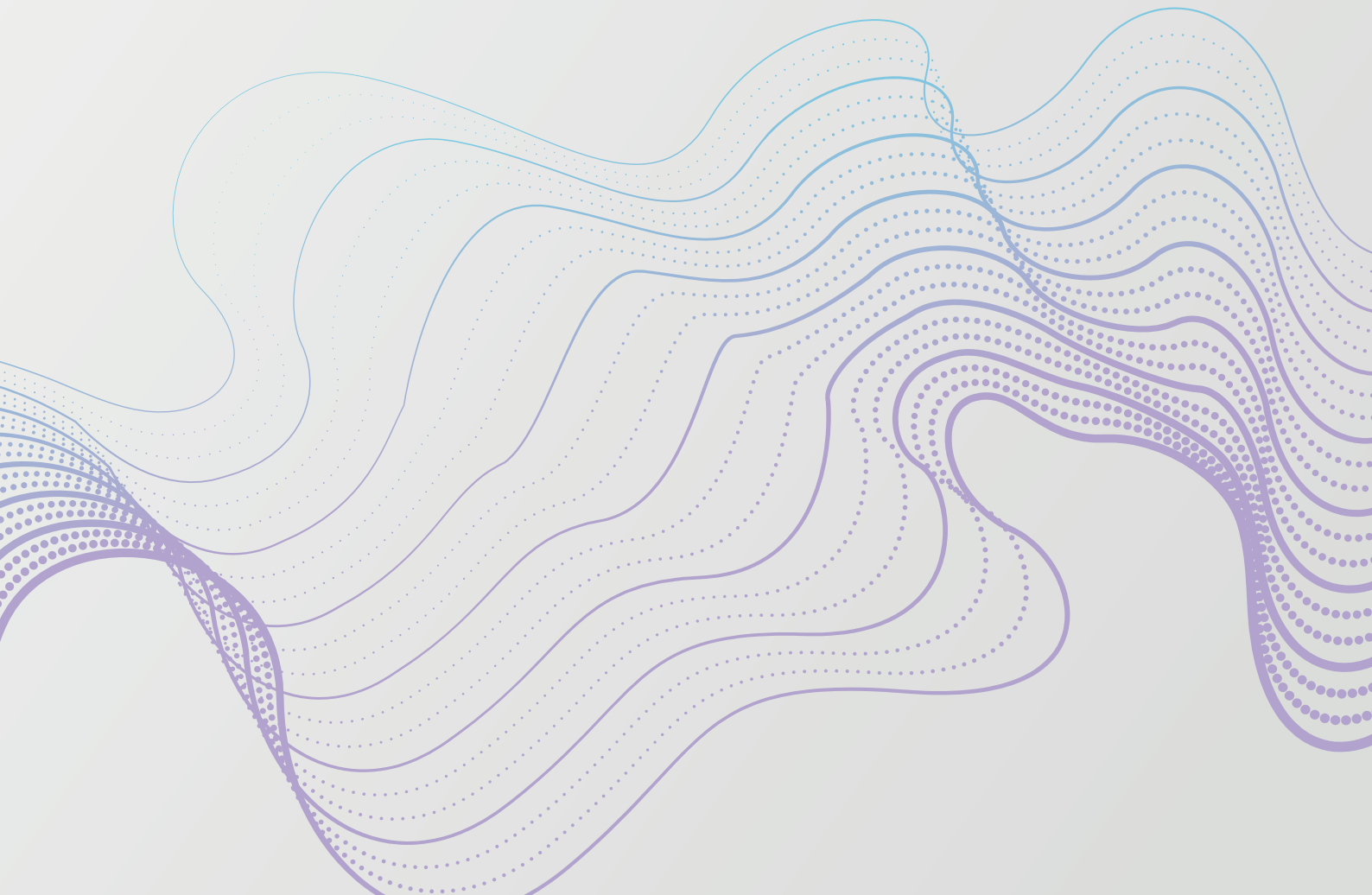




National Biofilms
Innovation Centre

The Need for Funding in Biofilm Standardisation

NBIC POSITION PAPER





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Executive Summary

Microbial biofilms represent huge scientific and economic opportunities and are central to some of our most important global challenges – from antimicrobial resistance and food safety to water security and carbon emissions. Funding for biofilm standardisation projects is critical for advancing research and technology developments in these areas. By promoting consistency and standardisation, such efforts will drive innovation and have a significant impact on improving public health and the environment and on supporting multiple economic sectors.

The UK's National Biofilms Innovation Centre recommends that funders, standardisation organisations and regulators should take the following actions:

- Support the creation of a catalogue of standardised methodologies, validated and recommended by experts, which could be built e.g., under the umbrella of the British Standards Institute (BSI) and British Standards Online (BSOL).
- Put a strategy in place for the development of guidelines, validated procedures and standardised methods that account for the inherent complexity and variability of biofilms to support reliable and reproducible research and products across sectors.
- Recognise the importance of metrology and validation research, such as round-robin studies, and provide the necessary support and resources to conduct them successfully.
- UK Research Councils, especially Innovate UK, to provide a platform for industry and researchers to work together to support voluntary standardisation as an industry driven activity.
- Establish a funding programme, readily accessible to both academic researchers and industry to encourage and enable collaborative, interdisciplinary research and metrology, and support standardisation (prenormative and normative) activities.
- Encourage contributions from wider academic expertise, industry researchers and end-users to accelerate the development of standardised methodologies, especially in the areas such as biofilm-affected industries, where the need is strong, yet progress is very slow.

Biofilms are self-organised communities of microorganisms embedded in an extracellular matrix, playing a major role in the biology of the environment, both natural and engineered. They can present risks to human and animal health, introduce food safety problems, disrupt production from oil and gas wells and contaminate potable water supplies. They can also be useful. Wastewater treatment processes make extensive use of biofilms, they can increase the bioavailability of nutrients in the soil and seal cracks in borehole casings. Biofilms exert a significant economic impact on multiple sectors, estimated at US\$ 5tn p.a. industry base globally¹. They contribute to urgent global challenges, such as chronic infections and antimicrobial resistance, which could cost US\$100 Tn in world GDP and 10 M deaths per year by 2050². Management of environmental and industrial biofilms impacts multiple sectors, with the examples of global economic significance of biofilms estimated at the US\$91 Bn in consumer products industry, the US\$91 Bn foods industry or US\$117 Bn water and wastewater treatment sector¹.

Background: Need for biofilm standards - industry consultations

"The lack of fit for purpose biofilm standards is holding back industry innovation and failing to address major challenges (...)"

"The industry are challenged to make claims which will be accepted by regulators with no standard tests at present, as standards lag behind technology development. There is a need to act (...)"

NBIC Workshops Reports³

Standards are essential for ensuring the safety, quality, and consistency of processes and products, as well as promoting innovation and facilitating trade and commerce. By establishing clear standards and promoting best practices, industries can improve their competitiveness, reduce costs, and ensure that their products meet the needs of customers and regulatory bodies.

The UK's National Biofilms Innovation Centre (NBIC) has organised a series of workshops on Biofilm Detection, Engineering, Management, Prevention and Microbe-Metal Interactions³ providing a platform for academic experts and industrial practitioners to collaborate and address challenges and unmet needs. A recurring challenge identified by NBIC's academic and industrial partners is the prevalent absence of standardised biofilm models and measurement / test methods, highlighting the need for standardisation initiatives and regulatory guidelines across all biofilm research areas.

In addition, NBIC and the US Centre for Biofilm Engineering (CBE) held, recently, a focused workshop on biofilm regulations and standardisation for the medical devices and pharma sectors⁴. Over 40 representatives from industry, academia, metrology, standardisation, and regulatory bodies attended to map the current landscape, identify needs and trends, and establish a forward working group. The discussions highlighted a strong need for a comprehensive review of existing standards, methods, and practices to identify gaps and prioritise the development of necessary standards.

Problem: LACK OF STANDARDS IN BIOFILMS HINDERS INNOVATION



Most existing standards do not account for the presence of biofilms, which can lead to inadequate measures and responses in various fields, from healthcare to environmental management.



Validated methods and biofilm models are often lacking or are inadequately representing real-world scenarios, limiting their effectiveness in understanding and addressing biofilm-related challenges across various sectors.



There is lack of biofilm standards to support certain technologies what can create uncertainties in assessing their performance and safety when dealing with biofilm-related challenges.



The absence of biofilm standards directly supporting regulatory requirements can pose challenges for some industries, hindering their ability to adequately address biofilm-related concerns in products and processes.



The lack of standards can contribute to prolonged and expensive regulatory claim processes, and make it difficult for companies to demonstrate compliance and address biofilm-related issues efficiently.

Need: URGENT NEED FOR GLOBAL, HARMONISED BIOFILM STANDARDS AND REGULATORY GUIDANCE

Solution: MULTIDISCIPLINARY APPROACH AND GLOBAL COLLABORATIONS FROM UNDERPINNING SCIENCE TO REGULATIONS

Figure 1. The lack of biofilm standards and regulatory guidance slows down innovation.

The awareness of the need for standardisation in biofilms affected sectors has been increasing in the recent years. There are several international groups and initiatives aimed at driving progress in delivering industry-relevant biofilm standards. These include: the US CBE, who has successfully facilitated the acceptance of five biofilm methods that have been approved by the American Society for Testing and Materials International (ASTM); the Association for Materials Protection and Performance (AMPP), specifically SC 22 on Biodeterioration that are currently pursuing the development of five microbiology

standards, accounting for biofilms, specific to the area of microbially-influenced corrosion; Working groups from the British Standard Institute (BSI) under the CH 216 and CEN/TC 216 Chemical Disinfectants and Antiseptics, working in cooperation to determine the biofilm standards of immediate need for development; The International Biofilm Standards Task Group, a multi-centre collaboration between NBIC, US CBE, Singapore SCELSE and, European COST action AMICI, formed to guide the international development and acceptance of standardised biofilm models and test methods in healthcare, environment and industry.

Standards vs regulations

“Standards are one important regulatory tool. The importance of standards is growing with the increasing globalisation of commerce, the emergence of new technologies and the need for interoperability”.

UK Innovation Strategy⁵

Standards are not always compulsory by regulators, but they may be used as the basis for regulatory requirements. In some cases, regulatory bodies may require that companies comply with specific standards in order to meet certain regulatory requirements. For example, the US Food and Drug Administration (FDA) may require medical device manufacturers to comply with specific standards such as ISO 13485 to ensure that the devices are safe and effective. In other cases, regulatory bodies may refer to standards as a way to help companies understand and meet regulatory requirements but may not require strict adherence to specific standards.

Recently, to address the needs identified from stakeholder consultations, NBIC has commissioned a review on current methods used to support biofilm-related product claims and regulatory requirements

in the medical devices sector⁶. From the review, it is apparent that practically no particular biofilm standards or widely accepted standard methods exist, which would be endorsed or required by the regulations. New product claims are usually based, however, on several well-established methods for microbial investigations, with a clear potential to serve as basis for standardised methods or standards, that would be advantageous to the industry.

Standards often provide a level of consistency and clarity across an industry or sector. This can make it easier for regulators to assess compliance across a range of companies, as they can rely on established standards to provide a common basis for evaluation. From there, standards can be a valuable tool for companies looking to meet regulatory requirements in a timely and cost-effective manner.



Actions needed to address the need for biofilm standards

COMPLEXITY OF BIOFILMS HINDERS REPRODUCIBILITY OF METHODOLOGIES

"(...) support researchers to understand standards development opportunities and the growth opportunities afforded to businesses who can contribute to standards development in new and emerging markets by working closely with the BSI".

Innovate UK strategic delivery plan 2022 to 2025⁷

The inherent complexity and ubiquity of microbial biofilms makes it challenging to develop reproducible and standardised research models and methods. Biofilms can form on various surfaces and in diverse environments, resulting in significant variations in their structure, composition, and behaviour. This variability can hinder the development of consistent and reliable research models and methods. Moreover, the intricate interactions among microorganisms within biofilms can further complicate efforts to standardise research approaches.

STANDARDISED METHODS VS STANDARDS

Not always standards are necessary or practical. Considering the complexity of biofilm communities, their ubiquitous nature and the breadth of sectors affected, there is a general conviction that the creation of universal biofilm standards may not be feasible. However, a repository of standardised methodologies, validated and peer-reviewed, approved by the regulators and a guideline on how and when to use them would be very welcomed by the community. Examples of this kind of libraries exist in some areas already: UK Standards for Microbiology Investigations⁸ - a collection of recommended algorithms and procedures covering all stages of the investigative process in clinical microbiology, or the FDA's Catalogue of Regulatory Science Tools - a resource for medical device companies to use where standards do not exist⁹. The concept of a catalogue of biofilm-related standards methodologies has been reiterated recently by a panel of biofilm experts, in a publication, which followed a round table forum held at the 2021 International Biodeterioration and Biodegradation Symposium¹⁰.

RECOMMENDATION:

A strategy needs to be put in place by the policy makers for the development of guidelines, validated procedures, standardised methods that account for the inherent complexity and variability of biofilms to support reliable and reproducible research and products. It is essential to involve various stakeholders, including researchers, industry experts, regulatory bodies, and standardisation agencies, in the strategy development process. Collaboration will ensure that the perspectives and expertise of all relevant parties are considered, leading to a more comprehensive and inclusive approach.

RECOMMENDATION:

A catalogue of standardised and validated methodologies, recommended by experts and regulators could be built by the varied groups of stakeholders from academia, industry and public agencies, e.g. under the umbrella of BSI and BSOL (British Standards Online). Some methodologies could then serve as basis for the future quality / technical standards. Creating such catalogue for various aspects of biofilm research would provide researchers and industry practitioners with validated and peer-reviewed methods. This catalogue should cover a wide range of biofilm-related investigations, addressing different research and industry needs and application areas. Further, developing guidelines and best practices for biofilm research would provide researchers with a framework to approach their studies and experiments. These guidelines should address factors like sample preparation, experimental design, data analysis, and reporting, ensuring consistency and comparability across studies.

LIMITED FUNDING SLOWS DOWN PROGRESS IN BIOFILM STANDARDISATION

One major block to the establishment of biofilm standards or standardised methods is the lack of funding in this area.

There is a need for the funders to put money in and to promote the initiatives and projects, which are embedded in metrology and based on incremental developments supporting innovation (as opposed to blue-sky research, high-risk, transformative research).

The funding that exists is usually reserved to national metrology institutes (NMIs) and agencies, such as the UK's National Measurement System (NMS) laboratories, as a core funding provided in the UK by the Department for Science, Innovation and Technology (DSIT, former BEIS). There is also a funding from EURAMET, currently delivered through European Partnerships on Metrology Programme, directed at international collaborations, yet the budget is limited, and the bigger part is also given to the European NMIs and Designated metrology Institutes (DIs).

There are examples of projects that have dedicated part of their efforts to biofilm standardisation, yet they are very few and limited. They include the European Training Network PRINT-AID (that focused on anti-infective medical devices and had a work package dedicated to data integration and standardisation on biofilms); the EU project MetVBadBugs (EURAMET EMPIR Programme, aimed at developing quantitative measurements and imaging of drug-uptake by bacteria,

including in biofilms) and the NIST-funded project on "Biofilm Models to Evaluate Structure-Function Relationships" in the USA that is transversal in nature in terms of areas of application but that is focused on developing biofilm reactors.

Seldom grants are provided from the UK Research Councils, which would enable academics to pursue metrology and standardisation initiatives.

RECOMMENDATION:

Funding agencies have significant influence over research and innovation priorities and the types of research projects pursued. Establishing a funding programme that is accessible to both academic researchers and industry would encourage and enable collaborative, interdisciplinary research and metrology, as well as support standardisation activities. Such programme would help address industry sectors where the lack of standardised biofilm methodology is prevalent.

THE EXAMPLE OF ROUND-ROBIN STUDIES

Round-robin studies are a type of collaborative testing method where multiple laboratories or participants analyse the same set of samples to assess the accuracy and precision of a measurement method or analytical technique. These studies are crucial in ensuring the reliability and comparability of results across different laboratories and are often used to validate new methods or standards and play a critical role in advancing science and technology.

However, round-robin studies can be complex and time-consuming, requiring significant resources and coordination among the participating laboratories, often internationally. Also, because these studies usually involve collaboration across multiple institutions and organisations, finding funding and support for these studies can be challenging, and many studies rely on volunteers to participate.

IMPORTANCE OF METROLOGY AND VALIDATION RESEARCH

“Measurement can increase investment in R&D by giving confidence to investors, thereby de-risking the innovation journey. Measurement also helps to grow key hightech sectors by enabling companies to assure quality, comply with regulations and trade internationally”.

UK Measurement Strategy 2022¹¹

While metrology and validation research, such as round-robin comparisons, may not always be as exciting or attention-grabbing as more ground-breaking initiatives, they are essential components of scientific progress, and funding for such activities is crucial for continued advancement in a variety of fields:

- They can help build upon existing knowledge and advance scientific understanding in a particular field by making small, gradual improvements to existing ideas, technologies, or methodologies, rather than pursuing entirely new and revolutionary concepts.
- They can be more practical and more easily applicable than speculative research and can lead to tangible improvements in existing practices or technologies.
- They can help address specific gaps in knowledge or understanding that might not be as well-suited for more radical approaches.
- They can help validate or refine existing techniques or tools, deliver standards or standardised methodologies, which can be essential for advancing a field as a whole.

RECOMMENDATION:

It is important for funders and organisations to recognise the importance of metrology and validation research, such as round-robin studies, and provide the necessary support and resources to conduct them successfully.

Since metrology and validation research often involve collaboration between different laboratories and research centres, by enabling and encouraging such collaborations funders and organisations would promote knowledge sharing and facilitate the exchange of best practices and expertise, fostering a culture of continuous improvement and driving the adoption of standardised methods across the scientific and industry communities.

Biofilms standardisation in the UK

“Standards, measurement, and accredited conformity assessment play a critical role to support innovation and enable its swift and safe commercialisation”.

Standards for the Fourth Industrial Revolution¹²

We are on the right track to drive progress in the area of biofilm standardisation with the UK charging the initiative.

Encouraging is the increasing importance placed on standardisation in the UK's Government's plans, policies, and strategies over the past few years. In 2022 the Centre for Economic and Business Research Ltd (Cebr) estimated that a total of 23% of all UK GDP growth is attributable to the impact of standards and 38% of all productivity growth. Cebr estimated that standards have boosted the UK's annual GDP by £161 billion since 2000¹². The UK Innovation Strategy⁵ strongly emphasises the need for agile standardisation initiatives to enable regulations that can ensure the UK extracts the best value from innovation. The need is particularly explained in the UK's Action Plan on Standards for the 4th Industrial Revolution¹³. **Funders have an important role to play in supporting the development of research and industry standards,** and standardisation features strongly in the strategic delivery plans of the UKRI, especially Innovate UK⁷.

Standardisation process can take a significant amount of time, as it often involves extensive collaboration and consensus-building among stakeholders with diverse perspectives and interests. Depending on a sector, the process will require close cooperation with standardisation agencies, regulators, metrology centres, Catapults, KTN's and other networks.

The process of standardisation typically begins with identifying the need and gathering input from relevant stakeholders. This may involve conducting research, analysing data, and soliciting feedback from industry experts, regulatory bodies, and other interested parties.

The UK is well positioned to lead the advancement of standardisation in biofilm-affected domains.

Since its establishment, **NBIC has transformed the biofilm innovation landscape** in the UK, effectively creating an organised and curated connectivity between the UK's academic and industrial communities. This partnership encompasses 63 research institutions and over 150 actively involved businesses, resulting in the most extensive connected infrastructure for biofilm research and innovation worldwide. Furthermore, NBIC has established efficient processes for engaging national and international stakeholders, including collaborations with the UK's regulators, NMS laboratories, BSI, and government agencies, as well as other Knowledge Transfer Networks as needed. Additionally, international cooperation with other biofilm centres via the International Biofilms Standards Task Group and the European COST networks (i.e. AMICI¹⁴, Euro-MIC¹⁵) working towards biofilm standardisation brings, further, a global approach to harmonised standards.

RECOMMENDATION:

We urge the funders to establish programmes specifically directed at funding (prenormative/normative) standardisation research and activities, which would be readily accessible to academic institutions as well as industry. Currently the funding is rather obscure and goes mainly to the dedicated organisations specialising in metrology, standardisation, and regulations.

Enabling and encouraging the contributions from the wide academic expertise and industry researchers and end-users would accelerate the development of standardised methodologies, especially in the areas, such as biofilm-affected industries, where the need is strong, yet progress is very slow.

UK Research Councils, especially Innovate UK, could provide a platform for industry and researchers to work together to support voluntary standardisation as industry driven activity.

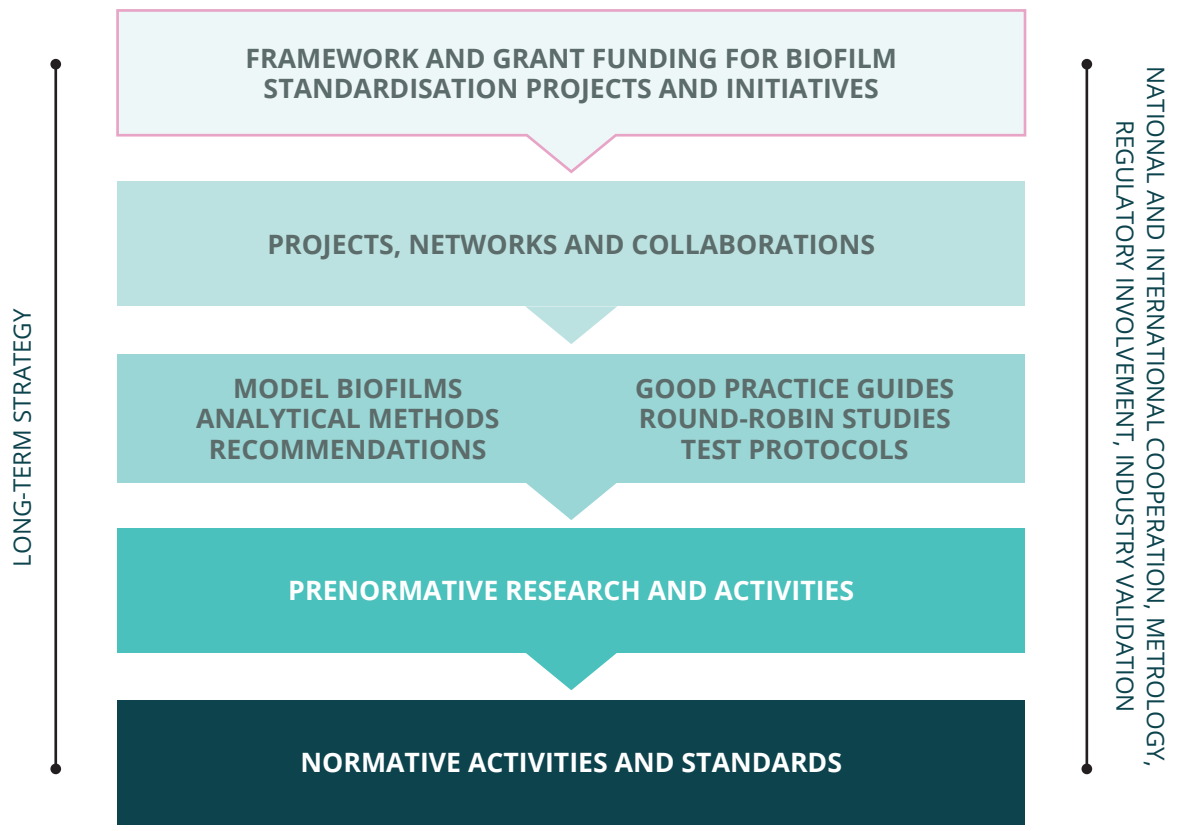
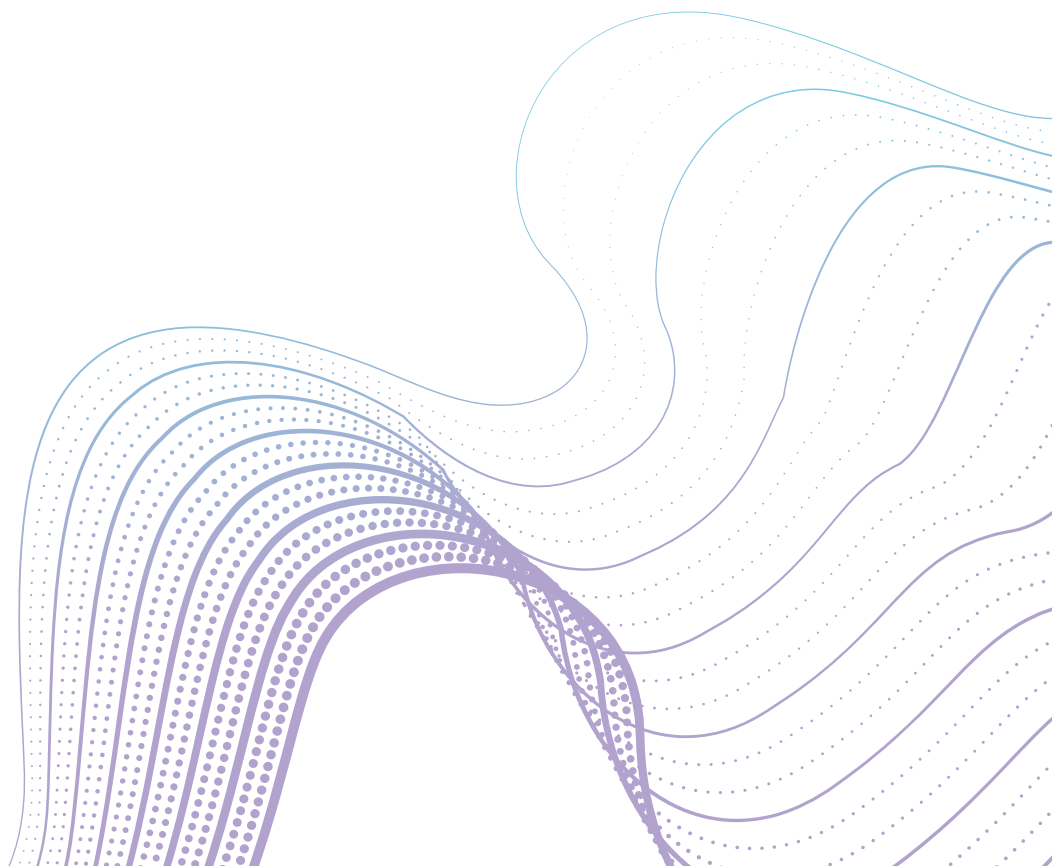


Figure 2. Underpinning role of funding needed to progress development of biofilm-related standards.



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National Biofilms Innovation Centre

The National Biofilms Innovation Centre (NBIC) is an Innovation Knowledge Centre (IKC) funded by BBSRC and Innovate UK. NBIC was launched in 2017 by its four lead Universities (Edinburgh, Liverpool, Nottingham and Southampton) and is led by four Co-Directors: Professors Cait MacPhee, Rasmita Raval, Miguel Cámara and Jeremy Webb respectively. With a consortium of 63 academic partner institutions across the UK, NBIC is the central hub where academia, industry, government and public policy come together to tackle the grand challenges biofilms present, impacting US\$5 trillion in global economic activity, from food and health to ships, clean water and energy. NBIC's mission is to establish a network of research and innovation capacity to catalyse partnerships with industry to achieve breakthrough innovations and impact.

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