BBSRC bioscience for the future

Innovate UK

EPSRC Engineering and Physical Sciences Research Council

Industrial Biotechnology Catalyst

Helping to commercialise UK biotechnology innovation

Funded Grants Rounds 1 - 4

INTRODUCTION

This document provides a brief description of the Industrial Biotechnology Catalyst mechanism, through which Innovate UK, the Engineering and Physical Sciences Research Council and the Biotechnology and Biological Sciences Research Council fund industrial biotechnology innovations within the UK.

Detailed herein:

- What the Industrial Biotechnology Catalyst aims to achieve
- The scope of this mechanism
- The funding streams that are available
- An analysis of applications in rounds 1, 2, 3 and 4
- A list of funded grants from rounds 1, 2, 3 and 4
- List of Collaborators

INDUSTRIAL BIOTECHNOLOGY CATALYST

The Industrial Biotechnology (IB) Catalyst will accelerate the commercialisation of industrial biotechnology-derived products and processes. It has been set up by Innovate UK, the Biotechnology and Biological Sciences Research Council (BBSRC) and the Engineering and Physical Sciences Research Council (EPSRC). A total of £75.6M has been awarded through 2014-2016.

HOW DOES IT WORK?

The Industrial Biotechnology Catalyst supports businesses and researchers in developing innovative solutions to challenges in industrial biotechnology and bioenergy. It funds projects that develop biological processes, or a combination of biological and chemical approaches, in:

- production of fine and speciality chemicals and natural products (for example fragrances, flavours, pharmaceutical intermediates)
- production of commodity, platform and intermediate chemicals and materials (for example plastics, resins and textiles)
- production of liquid and gaseous biofuels
- production of peptides and proteins (for example enzymes, antibiotics, recombinant biologics)
- novel or improved upstream or downstream processes to reduce costs or improve efficiency.

OUT OF SCOPE?

- The IB catalyst does not fund the research that uses feedstocks from material that could be used for the human food chain or animal feed for the purposes of production of liquid and gaseous fuels (unless they have already fulfilled their food purpose).
- Projects involving the production of food and drink are out of scope; however, projects may address the productions of fine chemicals for use as food ingredients, for example flavourings and colourings.
- The IB Catalyst does not support research aimed at discovery and screening for activity
- Projects involving the production of cell therapies and vaccine manufacturing are out of scope

EARLY STAGE: TRANSLATION

These academic research and development projects translate research discoveries into the development of industrial biotechnology processes or technologies.

Key features: Academic-led experimental work that builds on existing discoveries

Duration: three to five years
Total project costs: £2m to £5m
Academic funding: Only for organisations meeting BBSRC and EPSRC eligibility rule
Business partner funding: No funding is available but businesses are encouraged to join consortia, make contributions in kind and provide guidance and input.

EARLY STAGE: TECHNICAL FEASIBILITY STUDIES

These projects explore the commercial potential of an early-stage scientific idea through feasibility studies.

Key features: Projects can be business or academic-led

Duration: up to one year
Total project costs: up to £250k
Total research organisation costs: must not exceed 50% of total project costs
Business partner funding: Up to 70% of their total project costs for small enterprises, 60% for medium enterprises and 50% for large enterprises.

INDUSTRIAL RESEARCH

These projects build on recent discoveries to develop new technologies or processes. They should have already demonstrated feasibility at bench scale.

Key features: Projects must be business-led

Duration: up to three years
Total project costs: up to £5m
Total research organisation costs: must not exceed 50% of total project costs
Business partner funding: Up to 70% of their total project costs for small enterprises, 60% for medium enterprises and 50% for large enterprises.

LATE STAGE: TECHNICAL FEASIBILITY STUDIES

These projects allow businesses to test their proven process at a greater scale of operation or with commercially equivalent equipment for the first time.

Key features: Projects must be business-led

Duration: up to one year
Total project costs: up to £1m
Total research organisation costs: must not exceed 30% of total project costs
Business partner funding: Up to 70% of their total project costs for small enterprises, 60% for medium enterprises and 50% for large enterprises.

LATE STAGE: EXPERIMENTAL DEVELOPMENT

These projects allow businesses to demonstrate that performance seen previously is repeatable during extended testing at a commercial scale.

Key features: Projects must be business-led

Duration: up to two years
Total project costs: up to £10m
Total research organisation costs: must not exceed 30% of total project costs
Business partner funding: Up to 45% of their total project costs for small enterprises, 35% for medium enterprises and 25% for large enterprises.

BREAKDOWN OF ALL APPLICATIONS BY CHALLENGE AREA

Over three rounds of the IB Catalyst a total of 306 applications were received, totalling a request of £395.1 million. Within these, the applicants self-selected their challenge area, from the following:

- Proteins and peptides
- Fine and speciality chemicals and natural products
- Processes to reduce costs or improve efficiency
- Liquid and gaseous biofuels
- Commodity chemicals and materials

Figures 1 and 2 show a breakdown of the applications by challenge area. Applications have been received into all challenge areas, with the majority of applications being received in the fine and speciality chemicals and natural products challenge area.

Figure 1: Total number of applications (306)

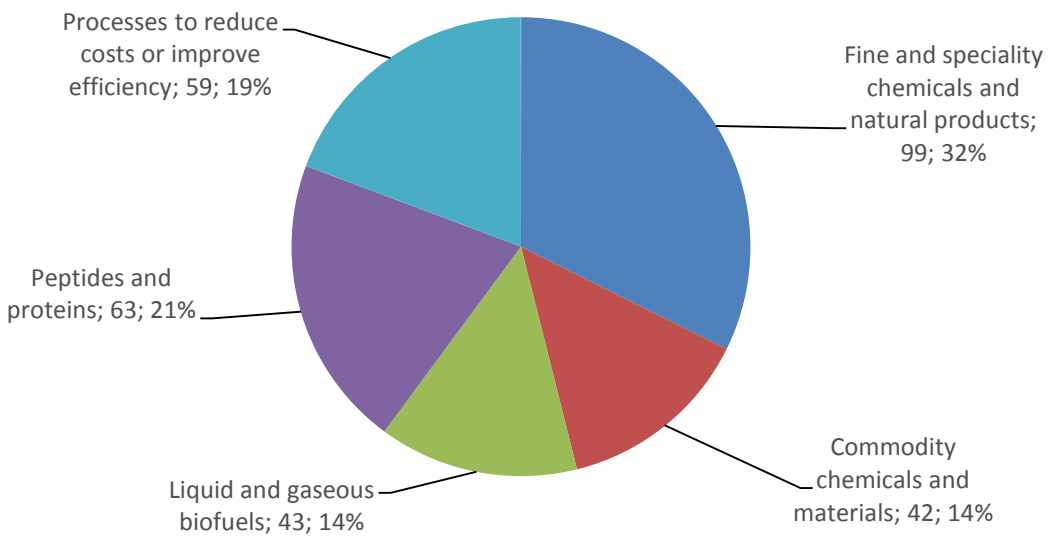
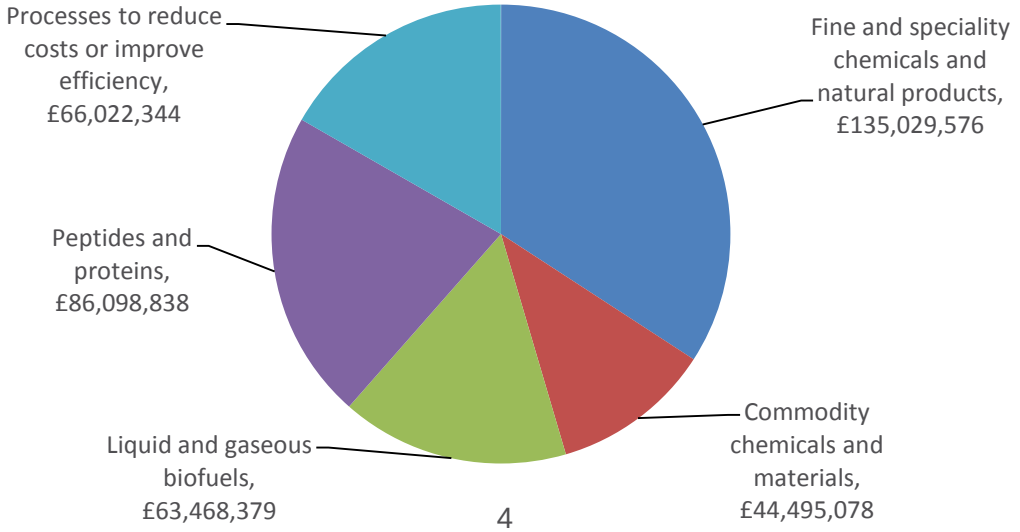


Figure 2: Total sought from IB Catalyst (£395.1 million)



BREAKDOWN OF FUNDED APPLICATIONS BY CHALLENGE AREA

Over the three rounds of the IB Catalyst a total of 82 out of the 306 applications have been funded, totalling £75.6 million. Figures 3 and 4 show a breakdown of the funded applications by challenge area.

Figure 3: Total number of funded applications (82)

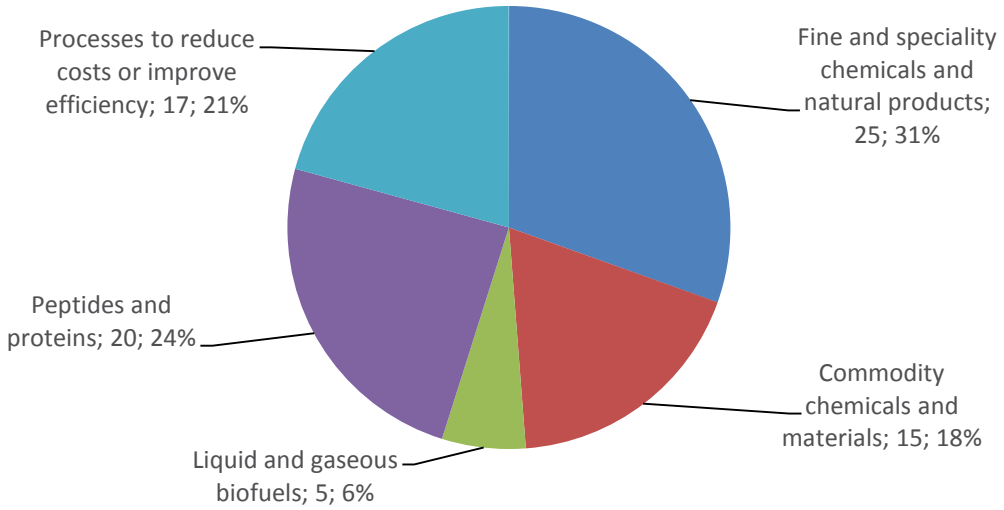
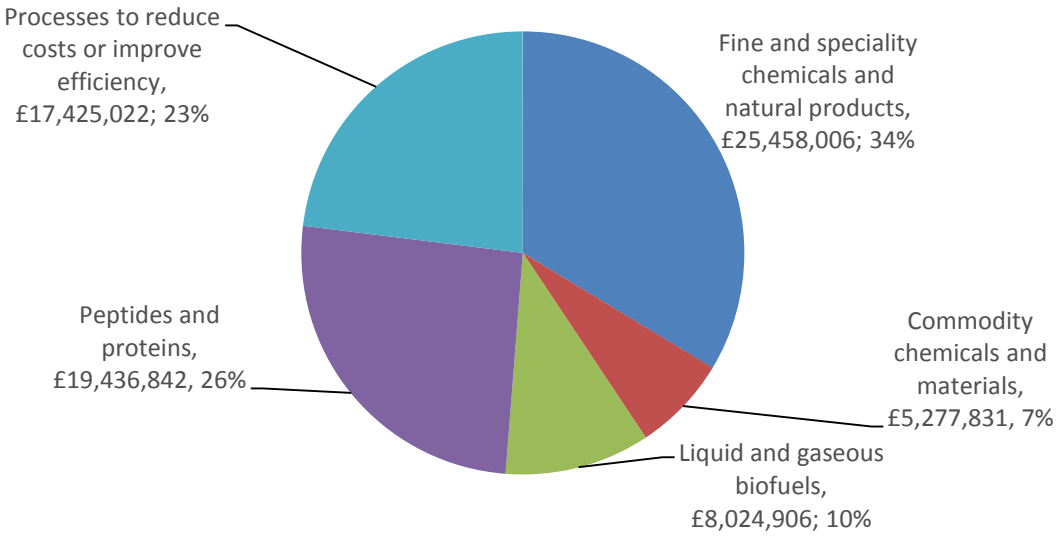


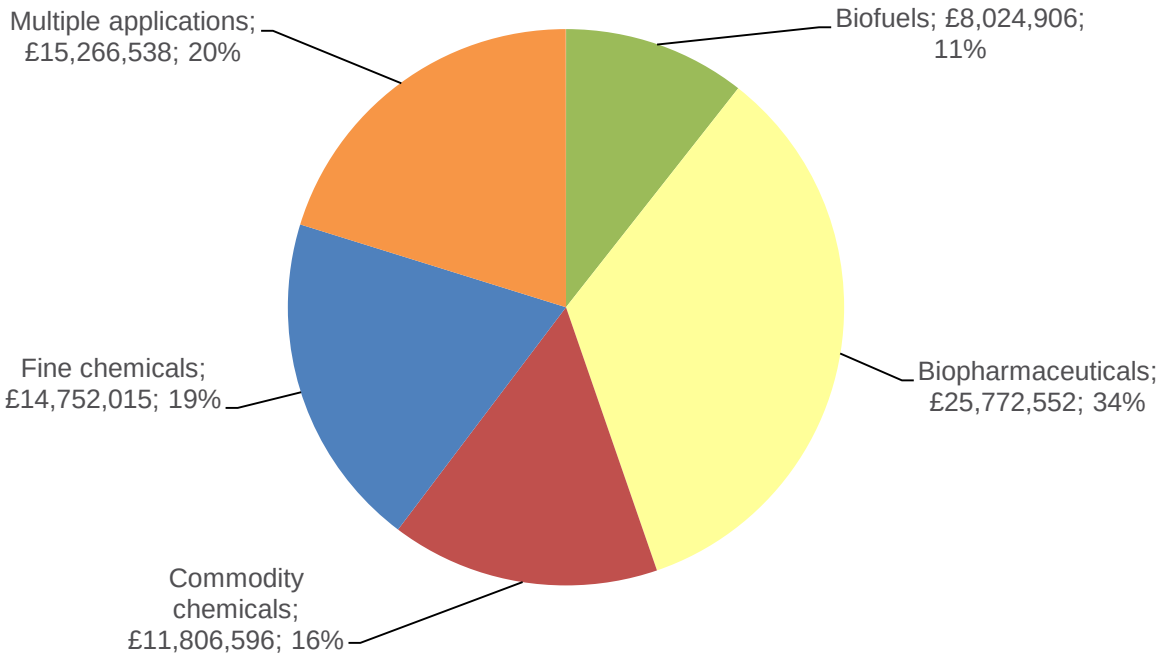
Figure 4: Total awarded (£75.6 million)



BREAKDOWN OF FUNDED APPLICATIONS BY END-PRODUCT SECTOR

Due to the broad scope of the 'processes to reduce costs and improve efficiency' challenge area as well as the self-selection of challenge areas, all applications were reclassified according to the sectors within which the end product of the research would fit. Figure 5 shows a breakdown of the 82 funded applications by end-product sector. The data shows that 34% of funded projects were associated with biopharmaceutical development and around 20% associated with developing technologies or processes that could have multiple applications.

Figure 5: Funding awarded (£75.6M)



BREAKDOWN BY COLLABORATION TYPE

Across the five streams of the IB Catalyst it is possible to apply with different combinations of collaboration types or as single applicants, however one of the aims of the mechanism is to foster collaborative working. The types of collaboration that we see in the IB Catalyst are listed below:

- Academic/Academic collaboration
- Academic/Industry collaboration
- Industry/Industry collaboration
- Single Academic Institution
- Single Industry Organisation

Figure 6 shows the numbers of applications received relating to each type of collaboration. The orange section of the column represents the number of funded applications and the blue section of the column represents the number of unfunded applications. On the top of each column is a value indicating the average score of applications in the category, showing that the Academic/Industry collaborations have scored higher on average than all other collaboration types. The percentage to the side of the column indicates the success rate by collaboration type, showing that the Academic/Industry collaborations have, to date, had the highest success rate.

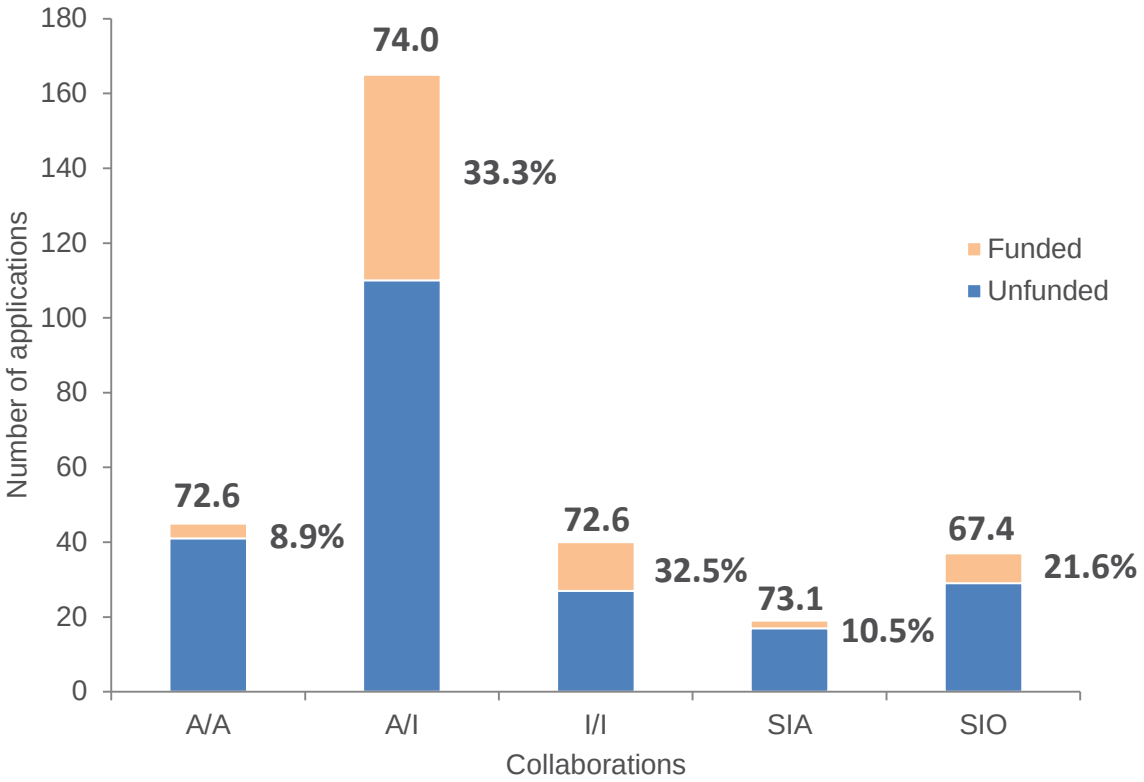


Figure 6: A breakdown of success rates by collaboration type

BREAKDOWN BY INDUSTRY INVOLVEMENT

Participants in the IB Catalyst mechanism representing the UK industrial community, come for a wide spread of company types; from the small or medium-sized enterprises (SMEs) to large national and multinational companies. The number of industrial and research and technology organisation (RTO)* partner involvements in IB Catalyst grant applications are represented, in Figures 7 and 8. The majority of the applications received through the IB Catalyst mechanism are from Small SMEs**.

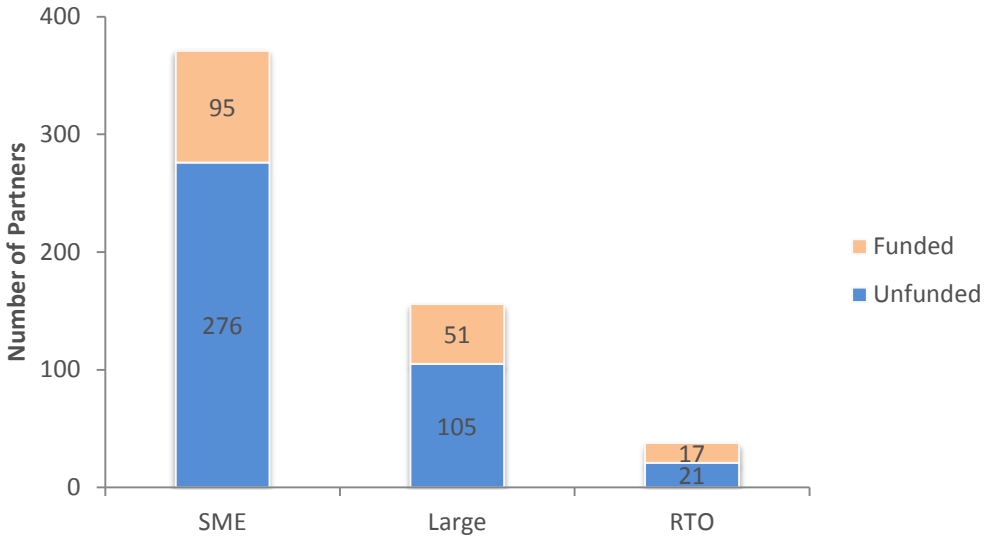


Figure 7: A breakdown of industry and RTO* involvements in IB Catalyst applications

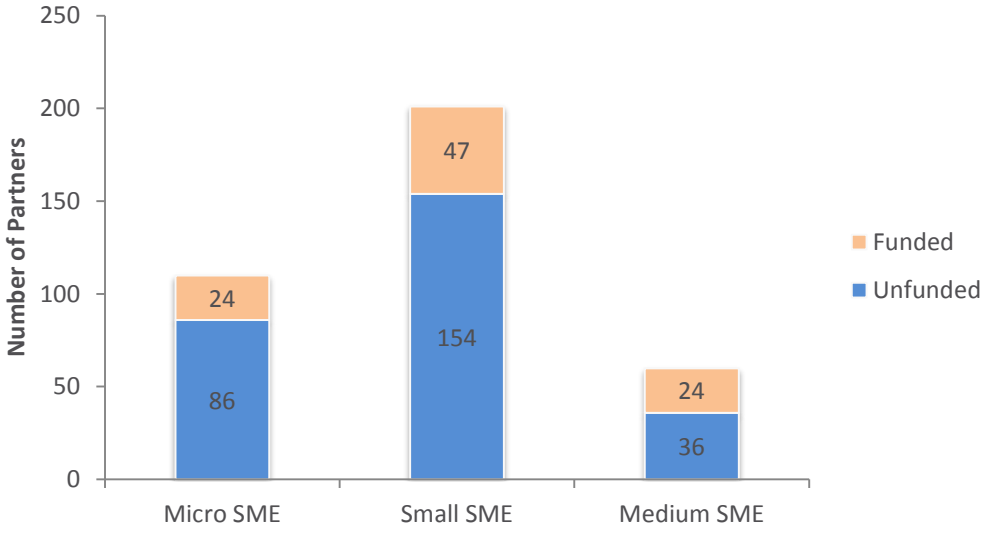


Figure 8: A breakdown of SME involvement in IB catalyst

* An RTO is a 'research and technology organisation' that predominantly provides research and development, technology and innovation services.
** Micro SMEs have a headcount < 10 and a turnover of < £2 million. Small SMEs have a headcount of < 50 and a turnover of < £10 million. Medium SMEs have a headcount of < 250 and a turnover of < £50 million

PORTFOLIO OF AWARDED GRANTS ROUNDS 1-4

A new generation of E. coli expression hosts and tools for recombinant protein production **Total Funding Awarded** - £2,024,903	
Challenge area – Proteins and Peptides	**Lead investigator –** Colin Robinson, University of Kent
Lead Co-I – Christopher Mark Smales	**Project partner institutions/companies (names) –** University of Birmingham (Timothy Dafforn, Steve Busby and Douglas Brown) and University of Sheffield (Philip Wright)
Numerous therapeutic biopharmaceuticals are produced in the bacterium *E. coli*, but current platforms have severe limitations and cannot produce many potential target molecules. This project aims to develop new platforms that directly address the major problems; (i) develop new expression systems that offer tighter product control, (ii) develop strains in which a wide range of products are exported to the bacterial periplasm by the Tat pathway, and (iii) apply a novel, rapid and cost-effective chemical-based method for releasing products from the periplasm. Each innovation will offer new tools and processes that render the new platforms more capable and cost-effective, and the 3 innovations will be combined to form a novel, integrated platform with powerful capabilities. The new systems will be validated by continual collaboration with a range of UK companies to ensure that they are fit for purpose.	

A Combinatorial Approach to Enhance Production of Monoclonal Antibodies **Total Funding Awarded -** £3,373,212	
Challenge area – Proteins and Peptides	**Lead investigator –** Robert White, University of York
Lead Co-I – Daniel Ungar and Nia Bryant	**Project partner institutions/companies (names) –** University of Edinburgh (Susan Rosser)
The CHO cell is the most widely used system in the biopharmaceutical industry for producing therapeutic proteins, but it can still struggle to express and secrete, at high levels and in a sustained manner, large biologics, such as monoclonal antibodies (mAbs). This problem will be addressed through a systematic combinatorial programme of synthetic cell engineering that combines innovative approaches to concomitantly increase mAb expression and secretion. The team combines complementary skill sets to focus on successive steps that are potentially rate-limiting for mAb production. Combining these strategies will produce CHO lines optimised to produce mAbs of great economic and therapeutic value. A robust, flexible and adaptable UK platform for optimisation and manufacture of therapeutic biologics will be established. This will benefit society, by decreasing production costs and thereby make more widely available therapeutics that currently are prohibitively expensive.	

Developing platforms for the production of diterpenoids **Total Funding Awarded** - £3,090,901	
Challenge area – Fine and speciality chemicals and natural products	**Lead Investigator –** Ian Graham, University of York
Lead Co-I – Margaret Smith and Andrew King	**Project partner institutions/companies (names) –** University of Cambridge (Alison Smith), University of Reading (Geoff Brown), Croda, GSK, and Unilever
Plants produce a wide range of diterpenoids, many of which are used commercially, such as a paclitaxel, (treatment of cancers), and steviol glyclosides (zero-calorie natural sweeteners). Many other useful diterpenoids cannot yet be commercially exploited due to their limited availability and/or high production costs. With synthetic biology, it is possible to engineer organisms such as yeast so that they are able to covert simple sugars to high-value chemicals. This project will develop “chassis organisms” that can be used for scalable diterpenoid production. These biological production systems will be useful in producing many diterpenoids that are found in nature, and the project will focus on two compounds which could be used in the treatment of cancers, or in skincare products such as sunscreens to protect skin against harmful UV light	

Manufacture of complex protein polymers for industry and medicine **Total Funding Awarded** - £1,819,746	
Challenge area – Proteins and Peptides	**Lead Investigator –** Jeremy Lakey, Newcastle University
Lead Co-I – David Fulton, Matthew German, Neil Perkins and Nick J Reynolds	**Project partner institutions/companies (names) –** N/A
Modern biomedical science and clinical medicine rely increasingly upon the growth of cells outside of the body. In this way animal free experiments can be performed which are highly informative about a range of diseases including cancer, arthritis and dementia. These artificial cell cultures can also be used to make new drugs and there is a growing industry making drugs such as Herceptin for cancer and vaccines against hepatitis. The hope of stem cells to create a range of regenerative medicine cures for a range of conditions now exists. In all these cases the cells are growing outside of the body and often require an external scaffolding of molecules to support their normal growth patterns. Currently these scaffolds are every expensive and of limited technical complexity. This project will create a cheap, pure and highly flexible source of polymeric proteins which can be built into a range of products to accelerate and stabilise the growth of cells in culture and assist all the technologies mentioned above.	

Improved downstream operation through formulation innovation **Total Funding Awarded** – £1,563,947	
Challenge area – Processes to reduce cost or improve efficiency	**Lead Investigator –** Nicholas J Darton, Arecor
Lead Co-I – N/A	**Project partner institutions/companies (names) –** Fujifilm Diosynth Biotechnologies and CPI
The aim of this project is to provide new formulations that bring about a step change in biopharmaceutical yield and quality by improving product stability through the most protein degradation sensitive/impactful areas of downstream processing (DSP). This is a novel approach to improving process efficiency as currently protein products have comparatively limited stability in the existing default DSP buffers. To develop a new platform of formulations and formulation strategies this collaborative project will bring together the formulation expertise of Arecor with the DSP expertise at Fujifilm Diosynth Biotechnologies (FDB) and The Centre for Process Innovation (CPI). The platform of formulations and the formulations strategies developed can then be applied to reduce production cost of all biologics to pharma and ultimately cost to healthcare providers. These new formulations may also enable the production of biotherapeutics that are currently very difficult/impossible to manufacture.	

Bioplastic polymers based on aromatic dicarboxylic acids derived from lignin **Total Funding Awarded** - £1,335,405	
Challenge area – Processes to reduce cost or improve efficiency	**Lead Investigator –** Paul Mines, Biome Technologies
Lead Co-I – N/A	**Project partner institutions/companies (names) –** University of Warwick (Tim Bugg), University of Leeds (Andrew John Blacker) and CPI
The environmental and social concerns surrounding the use of fossil fuels and food crops make lignin a compelling target as a source of chemicals. Considered of low commercial value, lignin is one of the few potential natural sources of aromatic chemicals. This project targets the useful aromatic building blocks for platform chemicals within lignin that can be substituted in plastics' intermediates. This project builds on a Technical Feasibility project undertaken by Biome Bioplastics and the University of Warwick, and seeks to demonstrate that metabolites extracted previously at laboratory scale can be produced in a commercially viable manner through the selective disintegration of lignin using bacteria and/or enzymes in fed batch/continuous reactors of scale. Larger trials will be undertaken at CPI and the resultant demonstration quantities of chemicals will be converted into novel materials, for evaluation in a high value market.	

ALGIPRO - Alginates by Production Scale Fermentation and Epimerisation **Total Funding Awarded** - £427,977	
Challenge area – Processes to reduce cost or improve efficiency	**Lead Investigator –** Sanantha Krishnan L., CPI
Lead Co-I – N/A	**Project partner institutions/companies (names) –** AlgiPharma AS and FMC Biopolymer
The project, ALGIPRO, is an innovative collaborative effort between Norway and the UK. It will translate over 20 years of academic research into an industrial scale production process for alginates. The Centre for Process Innovation Ltd. (UK) is leading the scale-up based on development by SINTEF (Norway). AlgiPharma AS (Norway) will use the product as the Active Pharmaceutical Ingredient in its development of medicines for cystic fibrosis, COPD and chronic wounds. FMC Biopolymer (UK, Norway) will market the product in existing and new applications within the food and pharmaceutical markets. If successful ALGIPRO will facilitate the introduction of novel medicinal products to the market that will ease patient suffering and potentially reduce healthcare costs. In addition it will be a new tool in fighting multi-drug resistant bacteria.	

Combinatorial genome editing to create enhanced biomanufacturing platforms **Total Funding Awarded** - £1,667,311	
Challenge area – Processes to reduce cost or improve efficiency	**Lead Investigator –** Mark Stockdale, Horizon Discovery
Lead Co-I – N/A	**Project partner institutions/companies (names) –** University of Manchester (Alan Dickson), and CPI
This project will deliver a pipeline of engineered Chinese Hamster Ovary (CHO) cells with characteristics and performance that will enable improved manufacture of novel biologic products. Recent research has identified critical metabolic check points that control CHO cell growth, and characterised pathways controlling product integrity and yield. In this project we will use this knowledge to deliver multiple and combinatorial gene 'edits' in CHO cells to produce cells that deliver efficiency and cost gains in manufacturing processes for biotherapeutic products, and broaden the product range that can be manufactured in this system. The improved performance of the cells will be assessed in fermenters and scaled-up to "manufacture ready" processes to ensure that project outputs are translatable into the manufacturing setting and outcomes are widely disseminated to the UK academic and commercial bioprocessing communities.	

Efficient production of first in class antimicrobial therapeutics from an integrated synthetic biology approach **Total Funding Awarded** - £417,092	
Challenge area – Peptides and proteins	**Lead Investigator –** Franck Escalettes, Ingenza
Lead Co-I – N/A	**Project partner institutions/companies (names) –** University of Plymouth (Mathew Upton)
Antibiotic resistant bacteria kill over 25,000 people a year in Europe and threaten a return to a time when minor infections can be fatal and routine surgery poses high risks. With development pipelines empty, there is a critical need for novel therapies to kill antibiotic resistant bacteria and serve as scaffolds for derivatisation, diversification and enhancement of efficacy, which proved successful with drugs like penicillin. This project will develop an exciting new class of antimicrobial biologics that rapidly kill bacteria, at very low doses and have great potential to prevent or treat bacterial infections including those caused by resistant bacteria. However, the development of the primary targets is hampered by their very low production in the native host and synthetic production would be prohibitively expensive. This project aims to develop efficient, adaptable and scalable microbial production systems for this novel compound class, enabling their development into a new platform of effective antibiotics.	

A naturally inspired industrial biotechnology route to the manufacture of a novel biopolymer with unique properties **Total Funding Awarded** - £300,518	
Challenge area – Fine and speciality chemicals and natural products	**Lead Investigator –** Ian Archer, Ingenza
Lead Co-I – N/A	**Project partner institutions/companies (names) –** Synthomer
Synthomer and Ingenza will continue the collaboration begun in a successful TSB co-funded Feasibility Study. Synthomer have identified a market gap for a product which if made using industrial biotechnology would have improved properties and none of the drawbacks of similar materials made by existing manufacturing technologies. It is anticipated that this product would be rapidly assimilated into one of their key market areas due the improved characteristics. Synthomer are a top 5 global supplier of emulsion and specialty polymer company with vast experience in this target market. Ingenza are a biotechnology enabler who develop novel bioprocesses using proprietary technologies. Ingenza will develop a bioprocess by creating a GM microorganism capable of manufacturing Synthomer's product. Following the successful completion of the programme, Synthomer and Ingenza expect to enter into a lasting collaboration to optimise a sustainable manufacturing bioprocess for this unique product.	

Industrial validation of nanofibre platform technology for biotherapeutics manufacture **Total Funding Awarded -** £1,658,246	
Challenge area – Processes to reduce cost or improve efficiency	**Lead Investigator –** Oliver Hardick, Puridify
Lead Co-I – N/A	**Project partner institutions/companies (names) –** University College London
Global demand for cheaper biotherapeutics, which represent many of the new tools in the fight against diseases such as cancer and neurodegenerative conditions, drives the need for a reduction in manufacturing costs. A significant proportion of current costs arise from the purification technologies used to ensure the safety and efficacy of these treatments. This project aims to build on existing collaborations between Puridify, an SME with a novel nanofibre purification technology, and University College London (UCL), a world leading research organisation for the development of industrial bioprocessing technologies. The successful award of this project lead by Puridify and supported by shadow industrial partners will see the development and commercialisation of innovative bioprocessing platform technologies allowing the cost effective manufacture of a wide range of existing and new products.	

Much-efficient and cost-effective manufacturing of antibody biotherapeutics employing integrated negative chromatography technology **Total Funding Awarded -** £720,536	
Challenge area – Processes to reduce cost or improve efficiency	**Lead Investigator –** Mariangela Spitali, UCB Celltech
Lead Co-I – N/A	**Project partner institutions/companies (names) –** BioToolomics
The current platform antibody purification process deployed in the bioprocessing industry becomes less efficient and less cost-effective to match with high titre upstream technologies. Based on previous feasibility studies using model antibodies, the key aim and objective of this project is to investigate negative chromatography based technologies using real industrial feedstocks to dramatically improve the overall process efficiency issue as described above. The market size in the downstream biopharmaceutical processing sector is circa $3 - 5 billion and it is a global market to play. The successful outcomes of this project will bring enormous potential cost benefits to the industry.	

Round 1 Early Stage: Technical Feasibility Studies

Development of superior Clostridial strains for low cost renewable chemical production **Total Funding Awarded** - £145,589	
Challenge area – Fine and speciality chemicals and natural products	**Lead Investigator –** Liz Jenkinson, Green Biologics
Lead Co-I – N/A	**Project partner institutions/companies (names) –** N/A
It is generally accepted that the manufacturing industry and the chemical industry in particular, needs to improve both the sustainability and the environmental impact of its products. However, although improved life cycle analysis (LCA) is important, the production cost and quality of renewable chemicals needs to be comparable with existing chemical products on the market. GBL is a UK-based industrial biotechnology company focussed on the conversion of sustainable feedstocks to produce renewable chemicals with a lower environmental impact than conventional fossil-carbon derived chemicals. Solvent producing Clostridia are excellent fermentation hosts for biobutanol and acetone but in this project we plan to develop novel Clostridial strains for different chemical products. We will capitalise on proprietary and ground breaking technology for genetic modification to develop novel Clostridial strains that ferment new substrates and produce high value speciality chemicals and food ingredients.	

Biochemical production of succinic acid from biorefinery glycerol: De-risking, scale-up, and feasibility **Total Funding Awarded -** £192,261	
Challenge area – Commodity chemicals and materials	**Lead Investigator –** Constantinos Theodoropoulos, University of Manchester
Lead Co-I – N/A	**Project partner institutions/companies (names) –** CPI, Brocklesby
This project addresses the production of succinic acid (SA), a top-added value chemical, through the fermentation of crude glycerol, the main biodiesel by-product. Currently, SA is manufactured from petrochemicals or by fermentation of glucose. The bioconversion of crude glycerol will valorise this renewable side-stream, significantly improving the biorefinery economy, and providing an economic, sustainable SA production route with reduced carbon footprint. A combination of experimental methods at a range of scales, computational tools, and market analysis will be employed in order to: prove the feasibility of the downstream process, benchmark the succinic acid product against market standards, optimise the scale up of the fermentation process and identify and engage commercial end users. The aim is to make a significant step in reducing the risk of the proposed bioprocess to attract industrial investments, hence moving closer towards its industrial uptake and application.	

Round 1 Early Stage: Technical Feasibility Studies

PeriTune - a clonal optimisation platform **Total Funding Awarded -** £217,231	
Challenge area – Peptides and proteins	**Lead Investigator –** Neil Dixon, University of Manchester
Lead Co-I – N/A	**Project partner institutions/companies (names) –** Cobra Biologics (Neil Dixon)
A variety of micro-organisms including *E. coli* and *S. cerevisiae* (baker's yeast), are used in commercial bio-production processes to manufacture a number of products, ranging from high-value low-volume products, such bio-therapeutics (e.g. recombinant insulin), to mid-value products, (e.g. biocatalysts and specialised chemicals), to low-value bulk commodity products (e.g. succinic acid and biofuels). This project seeks to develop a robust clone optimisation platform for the potential use and application in the above industrial sectors, and so would be of great benefit in a number of applied and fundamental areas of biological and biomedical R&D.	

Development of new tools for de novo polyketide synthase design **Total Funding Awarded -** £192,222	
Challenge area – Fine and speciality chemicals and natural products	**Lead Investigator –** Matt Gregory, Isomerase Therapeutics
Lead Co-I – N/A	**Project partner institutions/companies (names) –** University of Cambridge (Peter Leadlay)
Development of new tools for rational biological synthesis of novel natural products with potential use in design of improved anti-infectives, anticancer agents, agrochemicals and immune modulating agents.	

Round 1 Early Stage: Technical Feasibility Studies

Generation of a library of recombineered novel polyketides and non-ribosomal peptides **Total Funding Awarded** - £184,836	
Challenge area – Fine and speciality chemicals and natural products	**Lead Investigator –** Steven Moss, Isomerase Therapeutics
Lead Co-I – N/A	**Project partner institutions/companies (names) –** John Innes Centre (Barrie Wilkinson) and Biosyntha
Generation and analysis of a library of novel Natural Products using a new recombineering technology, with potential for use in pharmaceutical development, as treatments in indications such as infectious diseases, oncology and inflammation, as agrochemicals and fine chemicals.	

Discovery and development of large/diverse user-friendly panels of novel biocatalysts **Total Funding Awarded -** £152,628	
Challenge area – Fine and speciality chemicals and natural products	**Lead Investigator –** Simon Charnock, Prozomix
Lead Co-I – N/A	**Project partner institutions/companies (names) –** Northumbria University (Gary Black, Justin Perry and Meng Zhang)
This project aims to use cutting-edge high-throughput proprietary bioinformatics software, called "Filter-BLAST", in conjunction with the ever rapidly expanding DNA databases, to efficiently and accurately identify at the in silico level 500 key target enzymes, representing a diversity of 10 key biochemistries currently missing from the synthetic chemists enzyme toolbox. Advanced/proprietary high-throughput cloning technology (previously developed by Prozomix using TSB funds), called "GRASP", will then be used to rapidly clone the target genes selected and develop the encoded biocatalysts to cost-effectively populate 10 large/novel screening panels of key enzymes, and provide these materials to the biocatalysis community for screening towards specific individual biocatalysts of interest. After discovering enzymes fitting their exacting requirements, commercial quantities in animal-free, BSE-TSE certified form from Prozomix will be used to establish the new IB applications in the UK.	

Round 1 Early Stage: Technical Feasibility Studies

Engineering a Nano-factory for Peptide Synthesis **Total Funding Awarded** - £208,478	
Challenge area – Peptides and proteins	**Lead Investigator –** Mike Brownleader, Generon
Lead Co-I – N/A	**Project partner institutions/companies (names) –** University of Bristol (Steven Burson and Paul Race)
Peptides are short chains of simple chemical building blocks called amino acids. They are involved in numerous key biological processes including acting as toxins, pigments, drugs and hormones. They also control many of the most important cellular functions in animals, plants and man. There is considerable worldwide interest in developing new methods of producing peptides in sufficient quantity and of sufficient quality for use as pharmaceuticals, agrochemicals or research tools. The current favoured method for manufacturing peptides involves using chemical agents to fuse together the amino acid building blocks that form them. This approach is time-consuming, generates toxic waste products, and cannot be used for some valuable peptides. In this project, we will use an engineered peptide 'nano-factory' which when introduced into bacteria allows them to produce significant quantities of high value 'difficult' peptides without any of the problems associated with chemical synthesis.	

In vivo selection of bioprocessable biopharmaceuticals **Total Funding Awarded** - £205,143	
Challenge area – Peptides and protein	**Lead Investigator –** David Brockwell, University of Leeds
Lead Co-I – Sheena Radford	**Project partner institutions/companies (names) –** MedImmune and Avacta Analytical
Biopharmaceuticals (or biologics) are medicines that are made from biological materials, most usually proteins. The UK is a prominent stakeholder in this sector, which is growing in importance as biologics are often more specific to their target in the body and have fewer side effects. The development and production of biologics is, however, a labour and time intensive process. Many promising therapeutic proteins are never commercialised due to problems with self-association (aggregation). Failure of these 'candidate' therapeutics at a late stage of development is expensive to both industry and society as these therapies are usually indicated for serious life-threatening or life-limiting conditions. The aim of this project is to assess the ability of a screen developed by the applicants to identify candidate therapeutics at an early stage of development that are inherently resistant to aggregation. This would reduce the cost of development and reduce the failure rate of promising therapies for serious diseases.	

Round 1 Early Stage: Technical Feasibility Studies

Novel production processes for L-glufosinate **Total Funding Awarded -** £185,475	
Challenge area – Fine and speciality chemicals and natural products	**Lead Investigator –** Brian Green, Acidophil
Lead Co-I – N/A	**Project partner institutions/companies (names) –** N/A
Glufosinate is a £250 million dollar per year amino acid herbicide. It is currently produced as an even mixture of an inactive and an active form. Consequently, half of the product purchased and applied by farmers is inactive, wasting money and increasing the environmental load due to glufosinate use. Acidophil's innovation, to be evaluated in this early stage feasibility study, consists of developing technologies to produce only the active form of glufosinate, generating a product that should be cheaper and easier to use. Novel enzymatic steps, similar in concept to commercially proven processes, will be used to convert the inactive form into the active form. This project therefore represents applying an innovative technological approach to the production of a market-proven product.	

Novel platform biotechnology for the production of natural next generation 3D nanomaterials and nanodevices **Total Funding Awarded -** £206.863	
Challenge area – Fine and speciality chemicals and natural products	**Lead Investigator –** Eric. A. Whale, CelluComp
Lead Co-I – N/A	**Project partner institutions/companies (names) –** James Hutton Institute (Michael Taliansky and Andrew Love) and Mylnefield Research Services
Arraying of chemical groups and functional peptides on the surface of engineered, safe (non-infectious) virus-like nanoparticles (VNPs) permits the formation of biomimetic multifunctional and highly reactive nanoscale structures. This project seeks to develop the next generation functional 3D nanomaterials we via the incorporation of such multifunctional VNPs into a low cost nanocellulose matrix which has excellent mechanical characteristics, thus allowing production of innovative functional and catalytic nanoreactors, coatings, filters and other devices.	

Driving down the cost of waste derived sugar **Total Funding Awarded** - £601,522	
Challenge area – Commodity chemicals and materials	**Lead Investigator –** Nick Thompson, Fiberight
Lead Co-I – N/A	**Project partner institutions/companies (names) –** CPI, ReBio Technologies, University of Leeds (John Blacker), Aston University (Karen Wilson), Knauf and Novozymes
This project will build on UK expertise in recycling of household waste to recover a clean cellulose. A new process has been developed to efficiently break this cellulose down into sugar which can be used to produce, for example bioethanol - the green fuel component of petrol, as well as other high value chemicals such as those used in construction materials and intermediates in chemical processes. The sugar from waste will substitute for the sugar currently used which is produced from crops including sugar beet which requires land, pesticides and fuel to grow and harvest. The benefits are environmental, less waste to landfill, economic, the waste derived sugar is sustainable and cost competitive and social as land can be used for food grade sugar production instead of for the sugar required for fuel and other industrial purposes.	

Glycoenzymes for Bioindustries **Total Funding Awarded** - £3,190,711	
Challenge area – Peptides and proteins	**Lead Investigator –** Sabine Flitsch, University of Manchester
Lead Co-I – Nicholas Turner	**Project partner institutions/companies (names) –** John Innes Centre (Rob Field), University of Newcastle (Harry Gilbert), Institute of Food Research (Nathalie Juge), Ludger, and Biocatalysts
The use of glycoenzymes for advanced manufacturing and diagnostics will be increasingly important as biopharmaceuticals, functional foods, and bio-based products come to dominate their respective markets. Currently use of glycoenzyme biotechnology is limited by the availability of enzymes which are fit for industrial purposes and readily available. A wealth of enzymes and know-how exists in UK academia, potentially transforming industrial processes if these are translated into industrial applications. This project will develop an expanded toolkit of glycoenzymes which can be produced at scale and which satisfy the requirements of industry. Approximately 1000 different enzymes will be produced along with a comprehensive database of benchmarked performance data, and selected examples will be produced at industrial specification for evaluation by industrial partners. This project will increase the use of glycoenzymes, shaping future R&D and transforming industrial processes.	

Chemo-enzymatic Production of Specialty Glycans **Total Funding Awarded -** £3,525,991	
Challenge area – Fine and speciality chemicals and natural products	**Lead Investigator –** Bruno Linclau, University of Southampton
Lead Co-I – Seung Lee	**Project partner institutions/companies (names) –** University of Bristol (M. Carmen Galan), Open University (Sarah Ann Allman), University of Leeds (Bruce Turnbull), University of Warwick (Matthew Gibson), University of Manchester (Sabine Flitsch), University of York (Martin Fascione), Imperial College London (Ten Fenzi), Carbosynth, Dextra, Prozomix, Ludger and GSK
This project will investigate the enzymatic glycosylation of modified carbohydrate monosaccharides to achieve larger, biologically relevant glycan structures. This will be achieved by extensive screening of glycosyltransferase enzymes (enzymes that catalyse the addition of a new monosaccharide to a growing sugar 'acceptor'), that are able to use modified sugars as the 'acceptor', but also as 'donor'. The biological relevance of the synthesised new type of glycan structures will be validated by investigating their binding profile to a range of proteins that are known to be of relevance in the health sciences, with the immediate aim to develop new diagnostics applications. However, depending on the array results, further applications in other areas in the health sciences are envisaged.	

Large scale lentiviral vector production **Total Funding Awarded** - £2,315,688	
Challenge area – Peptides and proteins	**Lead Investigator –** Martin Pule, University College London
Lead Co-I – Adrian Thrasher, Waseem Qasim, Tasuhiro Takeuchi, Pamela Tranter	**Project partner institutions/companies (names) –** Kings College London (Farzin Farzaneh and Lucas Chan), and NIBSC (Mary Collins)
While modern medical therapies are currently based on small chemical drugs or protein based drugs, several new treatments are being developed where the therapeutic is a living cell. These therapeutic cells can be used for many disease including cancer and may be able to treat disease which chemical or protein drugs cannot. In order to manufacture many of these new cell therapies, genetic engineering of these cells is needed. h The best way to do this is to use a modified virus which comes from HIV. This virus is engineered so it cannot divide, but adds the new desired gene into the cell (and is known as a lentivector). Although this approach works very well, it is difficult to manufacture very large quantities of lentivector. A few years ago, many of the cell therapies were highly experimental. However,since some of these therapies are working well in patients, there is a considerable demand for lentiviectors. This project aims to find a way of large-scale production of lentivector.	

Biomethanisation of CO2 in anaerobic digestion plants **Total Funding Awarded** - £1,861,999	
Challenge area – Liquid and gaseous biofuels	**Lead Investigator –** Charles Banks, University of Southampton
Lead Co-I – Sonia Heaven and Yue Zhang	**Project partner institutions/companies (names) –** University of York (James Chong and Jane Thomas-Oates), University of Leeds (Mohammed Poukashanian, William Nimmo and Mark Walker), United Utilities, ITM Power, EverGreen Gas, and Food and Environment Research Agency
The research will create a hybrid anaerobic digestion process in which hydrogen made from renewable energy sources is used to produce biomethane at more than 95% purity. The process therefore provides an efficient in situ biogas upgrading technique which will maximise the conversion of the available carbon in waste biomass into a fuel product that has a wide range of applications, including short-term storage for grid balancing and use as a vehicle fuel. The process is likely to be more environmentally friendly and sustainable than current methods for biogas upgrading as there is reduced process loss of methane. The target is to develop the system for use in the water industry where there is a large potential to integrate it into existing infrastructure and to maximise the use of process heat and other by-products. A second targeted application is at a smaller scale on farms, where there is an abundant supply of waste biomass and a lack of suitable biogas upgrading plant.	

Commercialising thermo-stable rapeseed oil for the bio-lubricants industry **Total Funding Awarded -** £690,172	
Challenge area – Commodity chemicals	**Lead Investigator –** Keith Norman, Velcourt
Lead Co-I – N/A	**Project partner institutions/companies (names) –** University of York (Ian Bancroft), Biorenewables Development Centre, and Limagrain
Oilseed rape is the UK's third largest crop. As well as being edible, rapeseed oil is used extensively in biodiesel. There is potential for higher-value industrial uses, for example in applications such as lubricants and hydraulic fluids, to which it brings advantages of low toxicity and biodegradability. However, rapeseed oil is thermally unstable, due to a high content of polyunsaturated fatty acids. Recent advances in predictive mutation breeding have led to the development of oilseed rape lines in which this problem has been solved. To overcome the final hurdle to commercialisation, we aim to characterise temperature responses in controlled environments of a range of these lines and investigate more closely the agronomy of these new varieties through field trials, to maximise oil content and seed yield Whilst doing this, we will produce sufficient quantities of the new types of rapeseed oil to distribute to commercial users for evaluation.	

Developing a Quorum Sensing system into an efficient and economical way to control industrial production of high value products **Total Funding Awarded** - £1,388,169	
Challenge area – Processes to reduce cost or improve efficiency	**Lead Investigator –** Ben Huckle, GSK
Lead Co-I – N/A	**Project partner institutions/companies (names) –** University of Birmingham (Chris Thomas)
Natural or engineered biosynthesis can replace chemical synthesis with more environmentally friendly, sustainable bio-manufacturing processes to generate small molecule products such as pharmaceuticals. Although expression systems for recombinant proteins have been developed for laboratory scale and for commercial expression of very high value products such as antibodies, these are often unsuitable for industrial manufacture at scale and rarely appropriate for construction of recombinant biosynthetic pathways. The most significant gap is in mechanisms for control of gene expression, essential to turn a laboratory concept into a working, scalable bioprocess. Natural cellular systems have very sophisticated control mechanisms, one of which we propose to exploit as an induction free, highly efficient system for industry, equally capable of expressing single enzymes or large metabolic pathways.	

Enhanced productivity and functionality of Modified Ribosomally Produced Peptides (M-RIPPs) **Total Funding Awarded** - £1,290,261	
Challenge area – Peptides and proteins	**Lead Investigator –** Ian Fotheringham, Ingenza
Lead Co-I – N/A	**Project partner institutions/companies (names) –** Aberdeen University (Marcel Jaspers and Wael Houssen) and University of St. Andrews (James Naismith)
Ribosomally Produced Peptides (RIPPs) are widely recognised as one of the most promising classes of compounds with the potential to treat many diseases including infection, cancer & inflammation. They are of great interest to the pharma industry, but are extremely costly to produce/modify - even in milligram amounts. Through the utilisation of cutting-edge techniques in combinatorial synthetic biology, this project sets out to achieve a world first; namely, to produce bespoke libraries of Modified RIPPs (M-RIPPs) in sufficient quantities to permit drug discovery screening. The project combines the fundamental knowledge of the natural processes involved in RIPP biosynthesis of the two premier UK academic groups active in the field with the applied expertise in industrial biosynthesis of a leading UK IB company. It will deliver a versatile yet robust technology platform for the production of M-RIPPs that will be commercialised via a new UK spinout company.	

Industrial saponins **Total Funding Awarded** - £1,491,327	
Challenge area – Fine and speciality chemicals and natural products	**Lead Investigator –** Sarah Hosking, Unilever
Lead Co-I – N/A	**Project partner institutions/companies (names) –** John Innes Centre (Anne Osbourn), University of Edinburgh (Sarah Rosser), STFC – Laboratories (John Webster) and Croda
Saponins are soap-like substances or surfactants produced by certain plants. They have huge potential as a natural, biobased alternative to petrochemical surfactants for use in detergent products. However, extraction from plants is not economically feasible for use in detergents or sustainable on the basis of land use. This project sets out to establish a sustainable, commercially viable supply chain for the production of saponins in yeast. It tackles complex challenges of developing a yeast strain to produce the saponin at sufficient yield and how to recover the saponin from the fermentation medium. The project will also explore the physical properties of saponins alone and in mixtures with conventional surfactants, and will establish how best to formulate saponins into commercial detergent products for both economy and end results. Finally, the project will explore the safety of saponins using risk assessment methodology and in vitro methods.	

SeaGas : Production of bio-methane from seaweed by Anaerobic Digestion (AD) **Total Funding Awarded -** £2,072,745	
Challenge area – Liquid and gaseous biofuels	**Lead Investigator –** Linda Taylor, CPI
Lead Co-I – N/A	**Project partner institutions/companies (names) –** The Crown Estate, Queens University Belfast (Christine Maggs, Alberto Longo and Nessa O'Connor), SAMS (Maeve Kelly and Adam Hughes), Newcastle University (Gary Caldwell), Centre for Environment, Fisheries and Aquaculture,
This project will develop a process which uses seaweed for the generation of sustainable energy by anaerobic digestion (AD). Currently, farmers, food processors and industry use AD to generate bio-methane from wastes, to reduce energy costs or provide income. As waste supplies can be variable and AD is a continuous process, food crops like maize and beets are used to supplement waste. Seaweed has the potential to replace these food crops, which use land and water which could otherwise be used for human food production. The UK has extensive coastal waters and internationally recognised academic excellence in seaweed, its growth requirements and environmental considerations. This project brings together expertise in AD process development, economic modelling, environmental and social impact assessment and the supply chain - from seabed access for seaweed farming through to biogas injection into the national grid.	

Round 2 Early Stage: Technical Feasibility Studies

Fermentation of C1 feedstocks to 1,3-butanediol **Total Funding Awarded -** £163,138	
Challenge area – Commodity chemicals	**Lead Investigator –** Michelle Gradley, BioSyntha Technology
Lead Co-I – N/A	**Project partner institutions/companies (names) –** N/A
This process addresses the transfer of a novel unnatural metabolic pathway for synthesis of the 1,3-butadiene precursor 1,3-butanediol into microorganisms (acetogens) capable of fermentation of C1 feedstocks. The C1 feedstocks include syngas, which can be derived form most carbonaceous materials including dosmestic and industrial wastes. The ability to use methanol with CO2 or with syngas mixtures is also possible. A patent has been applied for to protect this invention and this project will ensure full and detailed exemplification of the technology.	

Maximising synthetic peptide and protein manufacture by in vivo DNA assembly in bacteria using high throughput robotics **Total Funding Awarded -** £186,677	
Challenge area – Peptides and proteins	**Lead Investigator –** Ryan Cawood, Oxford Genetics
Lead Co-I – N/A	**Project partner institutions/companies (names) –** N/A
Many different factors influence whether a piece of DNA will work in a biological setting, to express the protein it encodes. Proteins represent a broad new class of exciting but expensive new medicines. Poor DNA activity is particularly problematic when manufacturers of proteins need to produce large quantities by industrial manufacture. At Oxford Genetics we have developed a wide range of tools and expertise to allow us to design and build DNA sequences that produce high amounts of proteins. In this project we aim to industrialise a large proportion of our existing work flow and make the assembly of complex DNA an automated high-throughput process. This will enable the rapid and efficient development of DNA sequences that are optimal for producing proteins in any system, and should lead to major improvements in protein manufacture. This will benefit many aspects of commerce and medicine in the UK.	

Round 2 Early Stage: Technical Feasibility Studies

Industrial Platform Development for Commercial Enzyme Production **Total Funding Awarded** – £129,231	
Challenge area – Processes to reduce cost or improve efficiency	**Lead Investigator –** Mark Blight, Biocatalysts
Lead Co-I – N/A	**Project partner institutions/companies (names) –** Labgenius
Enzymes are biological molecules that facilitate chemical reactions in living cells. Many products in the food, fine chemical, flavour & fragrance, pharmaceutical and biotherapeutic industries use enzymes in their manufacturing processes. Many enzymes on the market are isolated from their original wild-type organism, many more need to be produced in a different host organism that is more suitable for large-scale industrial production and is capable of providing commercially viable yields of the enzyme. To optimise the level of production of the enzyme is time consuming and costly and often results in failure to achieve commercial yield targets due to the inherent biology of the host and the enzyme. Therefore, this project will develop a broad-host range expression system for expressing any new enzyme in a selection of industrially compatible microorganisms and assessing enzyme production in these multiple hosts prior to selecting the one that provides the highest yields for that enzyme.	

Ketoreductase Catalysed Manufacture of Active Pharmaceutical Ingredients **Total Funding Awarded -** £150,388	
Challenge area – Fine and speciality chemicals and natural products	**Lead Company –** CatSci
Lead Co-I – N/A	**Project partner institutions/companies (names) –** Prozomix
A consortium comprising of Prozomix, CatScI Ltd and Charnwood Technical Consulting has been established as part of the Innovate UK's IB Catalyst. The key goal of the project is to develop a technology platform for an IB route to active pharmaceutical ingredients to replace current processes manufactured through traditional chemical manufacturing techniques. The new technology has the potential to significantly reduce manufacturing costs whilst concomitantly allowing an increased output of the active pharmaceutical ingredient with a more robust supply chain. Additionally, this will have the added benefits of generating a more sustainable process as it will be more energy efficient and less reliant on hydrocarbon and precious metal based technologies.	

Round 2 Early Stage: Technical Feasibility Studies

Alternative synthesis of (–)-huperzine A with keto-reductases **Total Funding Awarded -** £174,784	
Challenge area – Fine and speciality chemicals and natural products	**Lead Company –** CatSci
Lead Co-I – N/A	**Project partner institutions/companies (names) –** Prozomix and Shasun Pharma Solutions Ltd
A consortium comprising Shasun, Prozomix and CatScI has been established as part of the Innovate UK's IB Catalyst. The key goal of the project is to develop a novel IB route to a nutraceutical that is currently manufactured through traditional chemical manufacturing techniques or isolated from scarce natural resources. The new technology has the potential to significantly reduce manufacturing costs whilst concomitantly allowing an increased output of the nutraceutical with a more robust supply chain. Additionally, this will have the added benefits of generating a more sustainable process as it will be more energy efficient and less reliant on hydrocarbon and precious metal based technologies. A successful project will allow the consortium to compete with manufacture in low-cost economies and help ensure that production of this critical nutraceutical continues in the United Kingdom.	

A Systems Biology Approach to the Optimisation of (Fed-) Batch and Continuous Fermentation Processes for Recombinant Protein Production **Total Funding Awarded** - £201,805	
Challenge area – Peptides and proteins	**Lead Investigator –** Ian Taylor, Chirotech Technology
Lead Co-I – N/A	**Project partner institutions/companies (names) –** University of Northumbria (Gary Black, Justin Perry and Meng Zhang) and Prozomix
The purpose of this feasibility project is to create a deep systems biology level understanding of the stresses placed upon an organism, under a range of (fed-)batch and continuous fermentation conditions required for the large scale and high titre manufacture of biocatalysts, through the use of the complex analytical techniques of metabolomics and proteomics. The project seeks to understand how variation in the genetic constructs and process conditions used to direct protein production can affect the organism and how these effects might be mitigated against, minimised and controlled by further re-design of the genetic components, feed medium and process conditions. The development of robust fermentation processes has economic advantages, through both cycle time reduction and raw material efficiencies and will have clear impact beyond this feasibility study through the reliable and more economic commercial supply of enzymes to Industrial Biotechnology using industries.	

Round 2 Early Stage: Technical Feasibility Studies

Improving the therapeutic window of glycosylated drug classes and the development of a novel, rapid, high throughput analytical methodology to streamline the drug development pathway **Total Funding Awarded -** £190,345	
Challenge area – Peptides and proteins	**Lead Investigator –** David Simpson, Glythera
Lead Co-I – N/A	**Project partner institutions/companies (names) –** GlycoSelect and CPI
Development of biotherapeutics is risky and expensive with current timelines from bench to bedside being estimated at 7-10 years at a cost of $2.8bn. This project exploits Glythera's technology which can stabilise glycosylation profiles to increase bioavailability and the therapeutic window to enhance the efficacy of the drug but also patient care through the reduction in dosing cycles. GlycoSelect will develop a highly specific lectin to Glythera's technology as a supporting and orthogonal approach to analytical development and characterisation. Since this rapid methodology can be deployed during any point in the discovery through to the clinical development programme this would support and significant de-risk drug development efforts. Both companies will demonstrate the value of their combined technologies through the further development of improved drug classes and comparison to known analytical methods underpinning their importance in drug development.	

Genome engineering and synthetic biology approaches for improving industrial CHO cell production of biologics **Total Funding Awarded -** £181,250	
Challenge area – Peptides and proteins	**Lead Investigator –** Tom Payne, Lonza Biologics
Lead Co-I – N/A	**Project partner institutions/companies (names) –** Imperial College London (Mark Isalan)
This project will aim to develop proof-of-principle approaches for improving CHO cell platforms for recombinant protein expression and bioproduction, based on combining: (i) rational site-targeted genome engineering (ii) gene circuit design, employing elements of genetic feedback regulation and conditional regulation. In this way, "difficult-to-express" proteins will be tested against a benchmark gold-standard expression protein, with the aim of improving protein production in a self-regulating, widely-applicable manner.	

Round 2 Early Stage: Technical Feasibility Studies

Optimisation of the Quorn fermentation process for the production and extraction of functional mycoprotein **Total Funding Awarded** – £206,227	
Challenge area – Peptides and proteins	**Lead Investigator –** Tim Finnigan, Marlow Foods
Lead Co-I – N/A	**Project partner institutions/companies (names) –** Heriot-Watt University (Stephen Euston and Nicholas Willoughby)
Food scientists at Heriot-Watt University have reported that proteins extracted from the Quorn fermentation process could be used to replace less sustainable proteins in food and biomedical applications animal proteins, as well as fat replacers. The researchers and Marlow Foods (producer of Quorn) team up again, this time to assess the feasibility of producing and extracting these proteins on a large scale. Ultimately these proteins could be used as natural foaming, emulsifying or gelling agents in innovative food and pharmaceutical formulations with environmental, health and economic benefits for society.	

Production of D-lactate in Geobacillus spp. **Total Funding Awarded -** £204,465	
Challenge area – Commodity chemicals	**Lead Investigator –** Ian Tebble, ReBio Technologies
Lead Co-I – N/A	**Project partner institutions/companies (names) –** University of Bath (David Jonathon Leak)
This project aims to produce modified strains of the microorganism Geobacillus to produce pure D-lactic acid for renewable products such as bioplastics using agricultural by-products and municipal waste. The bacterial host grows at high temperatures and has the ability to convert all the sugars in non-food materials, resulting in a process to produce D lactic acid directly via fermentation rather than current processes which require chemical conversion of L-lactic acid produced from food based feedstocks such as starch. The objectives of this work will be to demonstrate lab scale production of pure D-lactic acid from the modified Geobacillus strains and to design and demonstrate the industrial manufacturing processes. Finally the project will develop a business model and identify commercial partners for future Industrial Research grant applications.	

Round 2 Early Stage: Technical Feasibility Studies

Evaluation of the technical and commercial feasibility of the manufacture of bio-based polyester from cellulose derived 5-hydroxymethyl furfural **Total Funding Awarded** - £217,667	
Challenge area – Commodity chemicals	**Lead Investigator –** Paul Mines, Biome Technologies
Lead Co-I – N/A	**Project partner institutions/companies (names) –** University of Liverpool (Andrew Carnell)
Aromatic chemicals are a crucial constituent of plastics and bioplastics, conveying functionality such as strength and flexibility. At present, these chemicals can only be sourced economically from fossil-oil. However, lignocellulose is a potential low-cost and renewable input for aromatics both from lignin and indirectly from the cellulose portion. This project evaluates the commercial potential of novel work carried out at the University of Liverpool exploring aromatic chemical manufacture from cellulose. The project will evaluate sensitivity to feedstock type, improve reaction conditions and will be scaled to produce gram quantities. These chemicals will be converted into novel bioplastics and the properties of these materials tested. A techno-economic assessment of the overall process will be carried out to evaluate the commercial potential in both the bioplastic and broader plastics markets.	

Integr-algal **Total Funding Awarded -** £218,747	
Challenge area – Fine and speciality chemicals and natural products	**Lead Investigator –** J C Dodd, Algaecytes
Lead Co-I – N/A	**Project partner institutions/companies (names) –** University of Nottingham (Gillian Stephens and Anna Croft)
This project addresses the challenge of intensifying phototrophic algal production of high value natural products by integrating the it with downstream processing (extraction of Omega 3s from Algae). The aim is to produce high value Omega-3 polyunsaturated fatty acids (PUFAs), for use as active pharmaceutical ingredients (APIs) or food supplements. The novel process will, if successful, result in continuous growth of the algae, product formation and recovery. The new process will provide a commercially viable alternative to the extraction of PUFAs from fish, thus helping to provide a sustainable source for vegetarian consumers. The incorporation of Omega-3s (EPA and docosahexaenoic acid – DHA) into diet is relevant to the UK Government's strategy for well-being and maintaining the health of an increasingly aging UK population. The aging population in developing countries and dwindling oily fish supplies will mean a growing market for alternative sources of Omega 3 (EPA) in the next 25 years.	

Round 2 Early Stage: Technical Feasibility Studies

Clostridial on purpose acetone (COPA) **Total Funding Awarded -** £166,865	
Challenge area – Commodity chemicals	**Lead Investigator –** Liz Jenkinson, Green Biologics
Lead Co-I – N/A	**Project partner institutions/companies (names) –** Lucite International
There is large global demand for acetone for use as a solvent and in production of important chemicals and materials including transparent plastics such as methyl methacrylate (MMA). Acetone is currently produced by reacting petro-chemicals propylene and benzene, hence its price is volatile and the process is unsustainable. GBL are experts in clostridial (non-pathogenic) fermentation for production of the solvent n-butanol, which generates some acetone as a co-product. We (GBL and MMA-producer Lucite) undertook an InnovateUK business study to investigate potential for a process making solely acetone, and determined that this would be economically and technologically feasible. We want to use our expertise in clostridial biology to develop a strain of clostridia having high yield of acetone, necessary for the commercial process. Lucite will explore matters relating to use of bio-acetone for bio-MMA production.	

Chiral Chemical Synthesis in Clostridia **Total Funding Awarded -** £187,143	
Challenge area – Fine and speciality chemicals and natural products	**Lead Investigator –** Edward Green, CHAIN Biotechnology
Lead Co-I – N/A	**Project partner institutions/companies (names) –** N/A
CHAIN Biotech aims to produce high value fine chemicals (3-hydroxbutyric acid and ethyl-3-hydroxybutyrate) at costs lower then current chemical sysnthesis methods. By using microbial fermentation and renewable feedstock we also address key environmental and sustainability concerns. CHAIN has identified a new nutracetical market opportunity with TΔS who require lower cost ethyl-3-hydroxybutyrate to bring their new food ingredient to market. The over reaching goal is to capitalise on recent developments for genetic manipulation of Clostridium species to re-engineer industrially proven strains to produce high value chemicals instead of low value bulk chemicals. Success on this project would enable us to exploit the full potential of Clostridium bacteria for a wide range of IB products and applications.	

Round 2 Early Stage: Technical Feasibility Studies

Exploiting waste paper crumble using industrial biotechnology **Total Funding Awarded -** £189,889	
Challenge area – Commodity chemicals	**Lead Investigator –** Keith Waldron, Institute of Food Research
Lead Co-I – I Roberts	**Project partner institutions/companies (names) –** Palm Paper, Veriol Bio-Industries and Lenzing
The aim of this project is to exploit recent UK research to develop and evaluate the feasibility of a process to recycle 150,000 tonnes of waste paper crumble produced during the recylcing of waste paper. The crumble will be exploited for the component inorganic material. The organic cellulose component will also be used as a low cost source of glucose for producing platform chemicals and fuels. The outcomes will ensure added value, reduce carbon footprint of the process, and a reduction in disposal costs enhancing the competitiveness of the industry in the UK.	

Integrated energy efficient microwave and unique fermentation processes for pilot scale production of high value chemicals from lignocellulosic waste **Total Funding Awarded -** £3,260,364	
Challenge area – Fine and speciality chemicals and natural products	**Lead Investigator –** Christopher Chuck, University of Bath
Lead Co-I – Daniel Henk, David Leak, Rod Scott and Marcelle McManus	**Project partner institutions/companies (names) –** University of York (James Clark, Vitaliy Budarin and Avtar Marharu), Croda, C-tech Innovation and AB Agri
To meet key climate change targets, while providing sustainable economic growth, the UK must develop a robust bioeconomy. This requires the use of UK-specific agricultural waste streams. Currently, the expense and inefficiency of converting these feedstocks in to suitable sugars for fermentation has limited the growth in this sector. Recently, we reported an innovative one-step microwave process for the depolymerisation of bio-wastes. This key enabling technology achieves high sugar yields despite low energy inputs. Though a range of inhibitors are also formed in the process which limit the growth of most yeasts, we have shown that the robust yeast Metschnikowia pulcherrima (Mp) thrives on this feedstock to produce valuable 2-phenylethanol, arabinitol and a microbial oil akin to palm oil. Therefore this project aims to develop a pilot scale multi-product process by coupling these breakthroughs in low energy waste treatment and unique fermentation to produce value chemicals.	

DeTOX - Productive whole cell biocatalysis by engineering resistance to toxic products and substrates **Total Funding Awarded -** £3,097,444	
Challenge area – Processes to reduce costs or improve efficiency	**Lead Investigator –** Gavin Hugh Thomas, University of York
Lead Co-I – N/A	**Project partner institutions/companies (names) –** University of Nottingham (Gill Stephens), University of Sheffield (David J Kelly, Jeff Green and Susan Molyneux-Hodgson), University of Cambridge (Kathryn Lilley), Green Biologics, ReBio, Lucite, CPI and Ingenza
Product toxicity is a major problem for many IBBE processes involving production of small molecules by living cells. Toxicity causes yield restrictions & cell lysis, & frequently affects the commercial viability of biomanufacturing. Likewise, small molecules in lignocellulosic feedstocks inhibit bacterial fermentations & ultimately depress product yields. In this CBMNet NIBB-led bid, a team of scientists from four Universities apply their fundamental expertise in systems & synthetic biology & membrane function, to engineer increased resistance to small molecules in the industrially relevant bacteria, E. coli & solventogenic Clostridia. Our innovation is to translate BBSRC-funded research in microbial stress responses, membrane structure & membrane transporters, into the development & commercialisation of innovative applications in IBBE by our 5 commercial partners. A key project output will be a commercial chassis strain, DeTox, with generally increased chemical resistance.	

New Routes to Driving Enzyme-Catalysed Chemical Synthesis Using H2 Gas **Total Funding Awarded** - £2,911,050	
Challenge area – Fine and speciality chemicals and natural products	**Lead Investigator –** Kylie Vincent, University of Oxford
Lead Co-I – N/A	**Project partner institutions/companies (names) –** University of York (Alison Parkin)
This project builds up a technology that has the potential to make the production of fine chemicals such as pharmaceuticals, flavours or fragrances cheaper, faster, cleaner and safer. Chemists are starting to look to nature for more clever ways to make chemicals using enzymes isolated from the cells of bacteria and other organisms. One key barrier to using enzymes in making chemicals is that they often require helper molecules called cofactors which are used up during the chemical reaction. Since the cofactors are quite expensive, it is then critical to include a recycling system to provide a constant supply of the cofactor, but this usually introduces unwanted waste and side-products. We have developed a completely new approach to recycling the cofactors based on hydrogen gas - this allows very pure chemicals to be produced cheaply and with no waste. Of further benefit, we package the enzymes on carbon beads so they can be easily separated and re-used, making the process even more clean and economical.	

Improving the efficiency of Biocatalytic processes through the use of Electrodialysis systems (ImBioED) **Total Funding Awarded** - £308,280	
Challenge area – Processes to reduce costs or improve efficiency	**Lead Investigator –** Michael Lloyd, Chirotech Technology
Lead Co-I – N/A	**Project partner institutions/companies (names) –** C-tech Innovation
The ImBioED project seeks to deliver improved economics for the production and isolation of amino acids without the need for extensive plant modifications. We intend to achieve this through the integration of biocatalysis and electrodialysis (ED) technologies. Biocatalytic processes are frequently impeded by enzyme inhibition, which severely limits the scope for improving the volume efficiency of such processes. Building on promising results generated from a previous funded Innovate UK feasibility project we intend to utilise ED to remove inhibitory by-products from biotransformation processes, enabling us to achieve significantly improved levels of product accumulation.	

Pilot Algal Lipid Manufacturing in the United Kingdom (PALM-UK) **Total Funding Awarded -** £1,617,003	
Challenge area – Fine and speciality chemicals and natural products	**Lead Investigator –** Andrew Spicer, Algenuity
Lead Co-I – N/A	**Project partner institutions/companies (names) –** Rothamsted Research (Olga Sayanova), Plymouth Marine Labs (Mike Allan) and Stockton
A biorefinery uses biomass rather than crude oil to produce energy or chemicals. The term 'biorefinery' is routinely articulated in IB circles, but the concept has, as yet, never been fully realised. The objective of this project is to generate robust process economics for a fully-fledged biorefinery that will not just breakeven but moreover prove highly profitable. If successful, the project will then generate £24.5m investment from the Malaysian Govt. to realise the technology at scale. The project will involve functionalising microalgae to produce a range of products that can be separated using a low-cost continuous flow downstream processing system. It is innovative in that it will marry the best aspects of the conventional oil refinery (100% feedstock utilisation & high throughputs) with the best aspects of IB (functional complexity and environmentally benign processing).	

i-Bacillus: Adapting Bacillus licheniformis for 21st century IB applications **Total Funding Awarded** - £752,547	
Challenge area – Processes to reduce costs or improve efficiency	**Lead Investigator –** Frank Escalettes, Ingenza
Lead Co-I – N/A	**Project partner institutions/companies (names) –** Newcastle University (Colin Harwood)
Bacillus licheniformis is a preferred host for the production of industrial enzymes, including proteases for detergent and amylases and cellulases for food and biofuels. To advance its genetics/utility our key objective is to deploy SynBio tools to improve endogenous and heterologous enzyme production economics in B. licheniformis for exploitation via leading end users. Genome delivery technologies will amplify/target genes to locations validated for high-level/predictable expression, overcoming issues associated with non-targeted integration. Nuclease-based genome editing will a) address yield-compromising aspects of host metabolism under stress conditions identified through systems biology and b) capitalize on in situ protein engineering to improve endogenous enzyme function including thermotolerance and optimal activity under operating conditions. Success in these areas will reduce the cost and improve the versatility and efficiency of industrial enzymes produced in B. licheniformis.	

Development and optimisation of downstream processing for next generation biotherapeutics **Total Funding Awarded** - £1,341,947	
Challenge area – Processes to reduce costs or improve efficiency	**Lead Investigator –** Oliver Hardick, Puridify
Lead Co-I – N/A	**Project partner institutions/companies (names) –** University College London (Gary J Lye and Daniel Bracewell)
In recent years there has been rapid development of a “Next Generation” of protein-based therapeutics, yet the need remains for new manufacturing processes that can deliver these at a price healthcare providers can afford. For the first time these new therapies can safely modify a patient’s DNA, or harness the body’s own immune system, to treat inherited diseases, neurological conditions, and cancer. However, to achieve this clinical functionality the complexity and size of the therapeutic protein has increased. This has meant that existing purification technologies have been unable to be applied effectively in this new application. This project aims to build on existing collaborations and feasibility data to develop new purification tools and strategies that can be applied across a range of next generation biotherapeutics to enable their cost effective manufacture delivering novel therapies to patients at an acceptable price for healthcare payers.	

Enhanced Biofuel Production via Integrated Microbubble Technology **Total Funding Awarded** - £1,708,403	
Challenge area – Liquid and gaseous biofuels	**Lead Investigator –** Will Zimmerman, Perlemax
Lead Co-I – N/A	**Project partner institutions/companies (names) –** Suprafilt, Vireol Bio-Industries, Vivergo Fuels, Ensus and University of Sheffield (Robert Poole, Jeffrey Green and Will Zimmerman)
Global demand for cheaper biotherapeutics drives the need for a reduction in manufacturing costs. Rapid advances in recombinant production technologies are offering new therapeutic possibilities in the treatment of illnesses such as haemophilia, Parkinson's, and cancer. However, purification of these next generation protein therapeutics is extremely challenging due to the complex macromolecular nature of these structures. New purification processes are needed for these novel products to improve manufacturing efficiencies and economics. This is primarily a result of current chromatographic purification technologies being unable to effectively capture these large bioproducts, such as gene therapy vectors, which are much larger than current therapeutics. This project aims to build on existing collaborations and feasibility data to develop and commercialise an innovative bioprocessing technology to enable the cost effective manufacture of a next generation biotherapeutic.	

Round 3 Early Stage: Technical Feasibility Studies

Oscillatory baffled reactor for enhanced 1C gas bioconversion for energy production and storage **Total Funding Awarded -** £193,361	
Challenge area – Liquid and gaseous biofuels	**Lead Investigator –** Sandra Estevez, University of South Wales
Lead Co-I – Alex Zyh Siong Chong, Richard Dinsdale and Tim Patterson	**Project partner institutions/companies (names) –** NiTech Solutions Ltd
The production of green methane and carboxylic acids, by converting H2 using renewable electricity with surplus CO2 from a number of processes, has the potential to integrate gas, electricity and refuelling infrastructures, decarbonise energy supply, contribute towards energy security, as well as providing economic benefits through expansion of market potential. Combining H2 and CO2 has recently been achieved using a microbial process; however, productivity is limited by the rate at which gases can be solubilised into the liquid phase. This project will investigate the feasibility of using innovative oscillatory baffled reactor (OBR) technology to optimise the solubilisation of input gases, therefore optimising the rate of green gas or carboxylic acids production and improving the technical and economic viability of the biotech processes.	

Novel formulation design strategy **Total Funding Awarded -** £152,459	
Challenge area – Processes to reduce costs or improve efficiency	**Lead Investigator –** Dietmar Lang, Unilever
Lead Co-I – N/A	**Project partner institutions/companies (names) –** Imperial College London (Alfonso De Simone)
Bio-inspired processes will have a major impact on the global society in 21st Century. The employment of biocatalysts in industrial processes is expected to boost a sustainable production of chemicals, biopolymers, materials and fuels from renewable resources. The scope of this proposal is to translate academic research into industrial applications by exploiting techniques and methods developed in nuclear magnetic resonance of proteins to allow a new level of exploitation of biocatalysts in biotechnological processes and products. Among the large spectrum of applications, we will translate and apply this innovative technology to the accelerated design and creation of cold-cleaning formulations for reducing the environmental and economic costs of laundry.	

Round 3 Early Stage: Technical Feasibility Studies

Refining oxidative enzyme systems from talented microorganisms for industrial biocatalysis **Total Funding Awarded -** £212,408	
Challenge area – Processes to reduce costs or improve efficiency	**Lead Investigator –** Stephen Wrigley, Hypha Discovery Limited
Lead Co-I – N/A	**Project partner institutions/companies (names) –** University College London (John Ward)
Microorganisms and their cytochrome P450 (CYP) oxidative enzymes can be used for production of drug and agrochemical metabolites, or to produce new derivatives of early-stage lead compounds with improved properties. Hypha Discovery's panel of wild-type bacteria is highly effective in producing oxidized metabolites by whole-cell biotransformation but has limitations with regard to the speed and specificity of production. This challenge will be addressed in collaboration with UCL by introducing individual CYP enzymes from the six most talented members of the panel into E. coli and S. lividans chassis as three-gene operons using ferredoxin and ferredoxin reductase genes with broad functional activity. The catalytic activities of the resulting recombinant strains will be compared with those of the wild-type parents by testing against a diverse substrate panel. Cell-free enzyme extract preparations will then be prepared and assembled into a kit that can be used for testing in client laboratories.	

Quiescent Microbial Cell Factories **Total Funding Awarded** - £179,990	
Challenge area – Commodity chemicals and materials	**Lead Investigator –** Jeremy Bartosiak-Jentys, CPI
Lead Co-I – N/A	**Project partner institutions/companies (names) –** University of Cambridge (David Summers)
Many of the chemicals used to manufacture plastics, fuels and commodities are produced from microorganisms grown on various feedstocks in fermenters. This project will progress innovative patented technology which suspends unnecessary cell metabolism and growth while still enabling enhanced production of chemical products, a state known as quiescence. The advantages of quiescent cell technology (Q-Cells) are enabled for bioreactors operating under optimal production conditions with concomitant improved productivity, efficient and cost effective use of the feedstock and reduced waste generation. The mechanism to improve control of quiescence will be investigated within the constraints of industrial fermentation conditions under scale-down. This study will assess the generic applicability of the technology to improve competitiveness of Industrial Biotechnology to produce bulk chemicals.	

Round 3 Early Stage: Technical Feasibility Studies

Engineering Bacteria to Convert Methane into Poly Unsaturated Fatty Acids (PUFA) **Total Funding Awarded -** £212,332	
Challenge area – Fine and speciality chemicals and natural products	**Lead Investigator –** Ben Bradley, CHAIN Biotechnology
Lead Co-I – N/A	**Project partner institutions/companies (names) –** University of Nottingham (Nigel Minton and Ying Zhang)
In this project, researchers from CHAIN and the University of Nottingham aim to develop process technology that utilises methanotrophic bacteria to ferment methane into valuable nutritional supplements (lipids) for animal feed. Methane is a low cost and sustainable feedstock that can be produced from fracking or from a variety of renewable sources, including anaerobic digestion which is prevalent in the UK and Europe. Using specialist synthetic biology tools, the partners plan to engineer methanotrophs to ferment methane to produce a fish oil replacement in high yield.	

Novel Biocatalysts for Improved Routes to an Active Pharmaceutical Ingredient **Total Funding Awarded -** £152,054	
Challenge area – Fine and speciality chemicals and natural products	**Lead Investigator –** Nicholas Turner, University of Manchester
Lead Co-I – N/A	**Project partner institutions/companies (names) –** Chirotech Technology
The use of enzymes to catalyse reactions is a well-established technique used in modern organic chemistry as the use of biological catalysts can install unique and exquisite stereochemistry and regiochemistry into a synthetic route. This project will explore the development of two enzymes that catalyse important bond forming reactions in the synthesis of an Active Pharmaceutical Ingredient and their suitability for use as industrial biocatalysts.	

Round 3 Early Stage: Technical Feasibility Studies

AlgaeFlow – Novel acoustic microalgae harvester for sustainable biomass production **Total Funding Awarded** - £187,993	
Challenge area – Processes to reduce cost or improve efficiency	**Lead Investigator –** Devaki Bhatta, LabXero
Lead Co-I – N/A	**Project partner institutions/companies (names) –** University of Cambridge (Nigel Slater and Adrian Carl Stevenson), AlgaeCytes and Unilever
Although microalgal systems offer many advantages for chemical production (e.g. higher productivities per acre, valuable co-products), industrial-scale manufacture faces significant techno-economic challenges that must be overcome before algal biomass can be produced sustainably. To address this important challenge, this study investigates a cost-effective, energy-efficient in-line cell harvesting system based on innovative acoustic focusing, with a view to improving the efficiency and lowering the cost of commercial microalgae production by several orders of magnitude. This multi-disciplinary innovation is enabled only by converging cross-sector bio-sample extraction IP & world-leading bio-processing expertise with specialist algal product manufacturing knowhow. As a platform technology, applications exist beyond microalgal production for the wider benefit of industrial bioprocessing.	

Biotransformations of natural and inexpensive platform feedstocks to high value flavour compounds **Total Funding Awarded** - £153,716	
Challenge area – Fine and speciality chemicals and natural products	**Lead Investigator –** Charlotte Catignani, Treatt PLC
Lead Co-I – N/A	**Project partner institutions/companies (names) –** Northumbria University (Georgios Koutsidis and Gary Black)
The project focuses on biotranformations of relative inexpensive natural platform chemicals derived from distillation of essential oils and non-volatile compounds to higher value flavour compounds through biocatalysis. Experimental processes using a range of enzymes (P450s, KREDs and CCOs) from various sources have been previously described and a number of high value flavour components produced from inexpensive starting materials. In this project similar processes will be used to transform platform molecules using an array of enzymes focussed around those previously described. The flavour compounds produced will then be fractionated and assessed for their odour activity. Databases will be created to inform structure activity relationships followed by optimisation of reaction conditions and subsequent scaling to 1 L reactions	

Round 3 Early Stage: Technical Feasibility Studies

Feasibility study to determine whether a new generation of catalytic antibodies can be made that overcome existing limitations and are suitable for use in a range of clinical settings **Total Funding Awarded** - £179,815	
Challenge area – Peptides and proteins	**Lead Investigator –** Tom Crabbe, UCB Celltech
Lead Co-I – N/A	**Project partner institutions/companies (names) –** University of Manchester (Nigel Scrutton)
Antibodies, produced naturally in our bodies, have been successfully harnessed by the Biopharma industry to provide a whole new range of safe and effective treatments for unmet patient need. A good example is the anti-TNF antibodies, which are now in common use for sufferers of rheumatoid arthritis. Most therapeutic antibodies work by binding to a protein responsible for playing a role in the course of a disease, thereby stifling its ability to cause harm. This success means that a whole range of attendant technologies and know-how has been built-up to support therapeutic antibody R&D. For some time there has been speculation that if antibodies could be made to work as catalysts ("abzymes") then they could become even more efficient drugs. This Early Stage Feasibility Study will see scientists at UCB and Manchester Institute of Biotechnology collaborate in order to test whether the latest cutting-edge science is now able to make the breakthrough required for abzymes to at last fulfil their clinical promise.	

HydroBioChem: An innovative industrial biotechnology-drive route to commodity chemicals exploiting affordable but otherwise stranded hydrocarbon feedstocks **Total Funding Awarded -** £147,573	
Challenge area – Commodity chemicals and materials	**Lead Investigator –** Reuben Carr, Ingenza
Lead Co-I – N/A	**Project partner institutions/companies (names) –** N/A
The proposed project is aimed towards early stage feasibility research around the biomanufacturing of commodity chemicals through the development of a novel economically attractive bioprocess that will utilise advantageous/affordable hydrocarbon feedstocks. The project will be enabled by Ingenza's unique ability to readily discover, bioengineer and exploit hydrocarbon-utilising microorganisms.	

Round 3 Late Stage: Technical Feasibility Studies

Development of cGMP packaging cell lines for retro & lentivirus production using innovative molecular engineering strategies **Total Funding Awarded -** £491,267	
Challenge area – Peptides and proteins	**Lead Investigator –** Ryan Cawood, Oxford Genetics
Lead Co-I – N/A	**Project partner institutions/companies (names) –** University of Oxford (Leonard Seymour)
Recent advances in the treatment of a range of autoimmune diseases and cancer have required increasingly complex medical solutions. One rapidly expanding range of very successful treatments is the delivery of DNA to human cells (gene therapy) to provide them with new features and properties to help fight disease. A highly efficient method of achieving this is to use modified viruses, such as lentiviruses, to deliver the DNA. However, the process of making lentiviruses is highly inefficient because no cells have yet been made that allow the virus to be packaged efficiently. The reason for this is that some of the genes required to do this are toxic to the cell. We have recently developed a novel solution to this problem, and have already generated a first generation cell line that produces lentiviruses highly efficiently. We now aim to develop clinical grade versions of this cell line and create a series of further, more advanced, cell lines for improved lentivirus production.	

A Synthetic Biology Approach for the Total Biosynthesis of Semi-Synthetic Antibiotics **Total Funding Awarded -** £2,544,316	
Challenge area – Fine and speciality chemicals and natural products	**Lead Investigator –** Jason Micklefield, University of Manchester
Lead Co-I – Nicholas Turner	**Project partner institutions/companies (names) –** John Innes Centre (Barrie Wilkinson, Mervyn Bibb)
Natural products are molecules typically produced by plants and microorganisms that have been widely exploited for pharmaceutical and other applications. Often, these molecules nature provides do not have the required properties for use as therapeutic agents and further multi-step synthetic (chemical) transformations are required to produce a final optimised drug molecule. In this project, we are developing new enzymes which can be introduced into a host microorganism to produce the optimised drug molecule in a single-step fermentation process. Such a process will obviate the need for any additional synthetic transformations, which will reduce the environmental damage caused by typical chemical processes. Moreover, a single-step fermentation process will be more cost-effective, than existing synthetic processes, which will enable the cheaper provision of essential medicines	

New Enzymatically Produced Interpenetrating Starch-Cellulose Gels **Total Funding Awarded -** £2,736,276	
Challenge area – Fine and speciality chemicals and natural products	**Lead Investigator –** Stephen Eichhorn, University of Exeter
Lead Co-I – N/A	**Project partner institutions/companies (names) –** University of East Anglia (Yaroslav Khimyak, Jesus Angulo), University of Bath (Karen, Elder, Janet Scott), John Innes Centre (Rob Field), Unilever, Croda and AB Agri
Gels are used in a variety of commonplace products - from shampoos to mayonnaises. This project will develop a new range of gels of starch (from potatoes) and nanocellulose fibres using enzyme based processes. These gels will be produced at low cost and low energy with the end aim of use in the food and personal care products. The enzymes will assemble components into gels in the presence of water. Advanced techniques will be used to characterize mechanical and physical properties of the gels to explore their potential for these applications. We will add value to waste potato starch, making new products, reducing costs and CO2 emissions for the companies we will support through this technology. Industrial input will guide development of the gels, targeting key applications. Our approaches will have wide implications for the food and homecare industries, leading to greater use of gels and impacts on health and wellbeing.	

ConBioChem: Continuous bio-production of commodity chemicals **Total Funding Awarded -** £3,461,062	
Challenge area – Processes to reduce cost or improve efficiency	**Lead Investigator –** Gillian Stephens, University of Nottingham
Lead Co-I – Jon McKechnie	**Project partner institutions/companies (names) –** University College London (Gary Lye, John Ward), University of Cambridge (Stephen Oliver, Julian Griffin), Lucite International, Green Biologics, CPI, Ingenza and Chain Biotechnologies
The current slump in oil prices should not lead us to ignore the fact that, in the future, an ever-increasing proportion of fuels and chemicals, required by everything from jumbo jets to toy elephants, will need to come from renewable resources. This means a huge expansion of the fermentation industry, and the cost of the required manufacturing plant will rapidly become unaffordable. The solution is move from performing fermentations batchwise (like manufacturing cars one at a time) to continuous processes (like an automobile production line). This major change presents a number of challenges in designing and controlling the continuous industrial processes. This Project aims to produce a pipeline that will meet all of these challenges in an integrative manner, to provide stable and robust production microbes, a balance between microbe and product generation, new manufacturing processes and process controls that select for high-level production.	

MaxBio - Maximizing conversion yields in Biorefining **Total Funding Awarded -** £2,188,398	
Challenge area – Liquid and gaseous biofuels	**Lead Investigator –** Claire Halpin, University of Dundee
Lead Co-I – Robbie Waugh	**Project partner institutions/companies (names) –** University of Nottingham (Nigel Minton, Ying Zhang), University of York (Simon McQueen-Mason, D MacQuarrie), James Hutton Ltd, Chain Biotechnologies, Green Biologics and ReBio Technologies
In order to reduce greenhouse gas emissions and mitigate global warming while still managing to fuel and feed the world, many industries need to move towards using renewable carbon neutral feedstocks and away from using oil and petrochemicals. 'Bio'refineries making advanced transportation fuels and chemicals from plant biomass (i.e. agricultural wastes such as straw, or wood cuttings) have the potential to revolutionize the industrial landscape and make production of our fuels and chemicals more sustainable, but this will only succeed if sufficient value can be extracted from the feedstock to make the refining economically competitive with oil refining. This MaxBio project aims to improve the economics of biorefining by optimizing several different stages of the process in a holistic way that ensures that yields of end products are increased beyond what's currently possible.	

Translation of step-changing bioprocesses and expression system technologies for next-generation protein biologics production in CHO cells **Total Funding Awarded -** £1,209,967	
Challenge area – Peptides and proteins	**Lead Investigator –** Andy Racher, Lonza Biologics
Lead Co-I – N/A	**Project partner institutions/companies (names) –** University of Kent (Mark Smales)
Chinese hamster ovary (CHO) cells are the main production host for >US$145billion/yr of protein biologics used as medicines for a range of diseases. The CHO platform is mature when considering production of monoclonal antibodies, but new format non-native molecules such as fusion proteins, antibody fragments and other exotic molecules remain difficult to express (DTE) in this, or any other host. This project builds upon proof of concept work demonstrating that engineering the CHO chassis, together with growth media manipulation, increases both the yield and quality of a number of DTE proteins that are in development for application to unmet clinical needs and diseases with no current treatments. The project will advance the technology readiness level of our preliminary findings beyond proof-of-concept to deliver the commercialization of new CHO cell systems for DTE proteins and associated bioprocesses ready for industrial application to produce these important new medicines.	

Enhancing the yield of industrial Actinomycete fermentations **Total Funding Awarded -** £1,122,193	
Challenge area – Fine and speciality chemicals and natural products	**Lead Investigator –** Ben Huckle, GSK
Lead Co-I – N/A	**Project partner institutions/companies (names) –** University of Strathclyde (Paul Hoskisson)
Clavulanic acid (CA) is a beta-lactamase inhibitor able to potentiate the antibacterial activity of penicillins against otherwise resistant bacteria. It is the product of complex biological factories found naturally in Streptomyces clavuligerus, and is currently made industrially via fermentation using a strain that has been through successive rounds of natural selection. Fermentation conditions and media are carefully controlled and optimised to ensure maximum cell growth and CA production. A key condition is pH, which despite being controlled to ensure maximum cell productivity is conversely a major influence on degradation kinetics of the unstable CA molecule once produced. The proposed work aims to combine recent biological advances with industrial technologies to develop a strain and fermentation process designed to optimise yield while significantly reducing degradation. This project will provide a benchmark against which to judge the success of such an approach in an industrial environment.	

Enzymic polymerisation, characterisation and market evaluation of a set of novel bioplastic co-polymers derived from renewable resources **Total Funding Awarded -** £740,450	
Challenge area – Commodity chemicals and materials	**Lead Investigator –** Paul Mines, Biome Technologies
Lead Co-I – N/A	**Project partner institutions/companies (names) –** University of York (James Clark, Thomas Farmer) and University of Liverpool (Andrew Carnell)
The environmental and social concerns surrounding the use of fossil fuels and food crops make lignocellulose a challenging but compelling target source of high value chemicals. Previous and ongoing IB Catalyst studies undertaken by Biome, the Centre for Process Innovation and the Universities of Leeds, Liverpool and Warwick have demonstrated the feasibility of a bioprocess from lignocellulose to polyester pre-cursors. This project will seek to use industrial biotechnology (namely catalysis using enzymes) to convert these precursors into a suite of highly functional polyesters and understand their properties and lifecycle benefits. It will be undertaken by a consortium of Biome Technologies Ltd, the Universities of Liverpool and York. The project has the potential to advance the UK's knowledge and commercial position in the field of advanced bio-based materials.	

UK Continuous, Integrated Biologics Manaufacturing Project **Total Funding Awarded -** £ 1,437,419	
Challenge area – Peptides and proteins	**Lead Investigator –** Rob Noel, PALL EUROPE LIMITED
Lead Co-I – N/A	**Project partner institutions/companies (names) –** CPI, Allergan, Fujifilm Diosynth Biotechnologies, Medimmune, Sciex UK and Merck Sharp & Dohme
As biopharma moves to the business mainstream, the industry will increasingly need to find new ways to maintain competitiveness by ensuring affordability, quality, and delivery performance. Continuous processes have been proposed as a solution as they are scalable, offer higher productivity with reduced running times and materials usage, and require smaller footprint and less capital intense facilities. The project brings together five leading biopharmaceutical companies with UK Operations, process technology suppliers and a Catapult centre to develop an automated continuous biologics purification unit for more efficient manufacture of a wide range of biologic drugs. The new unit will consist of integrated, multiple operations running concurrently.	

Round 4 Early Stage: Technical Feasibility Studies

Recombinant expression of animal and plant phospholipases **Total Funding Awarded** - £89,604	
Challenge area – Peptides and proteins	**Lead Investigator –** Aelig Robin, Biocatalysts
Lead Co-I – N/A	**Project partner institutions/companies (names) –** N/A
Enzymes are biological molecules that facilitate chemical reactions in living cells. Many products in the fine chemical, food, flavour & fragrance, pharmaceutical and biotherapeutic industries use enzymes in their manufacturing processes. The majority (more than 75%) of enzymes currently used in industrial processes are hydrolytic in action. Among these, lipases and phospholipases are the enzymes that are used for lipid modifications. Phospholipases represent a versatile biocatalyst in various industrial applications. This project is aimed at producing phospholipases in simple microbial production hosts using recent technological advances in molecular biology in order to produce unique enzymes for the industrial biocatalysis market.	

Reducing contamination risk and increasing yields in the production of platform sugars from UK MSW **Total Funding Awarded** - £193,021	
Challenge area – Processes to reduce cost or improve efficiency	**Lead Investigator –** Nick Thompson, Fiberight
Lead Co-I – N/A	**Project partner institutions/companies (names) –** University of Southampton (Charles Banks), Novozymes US
Fiberight has created a circular economy solution to generate value-added products from municipal solid waste (MSW). The process involves thermo-mechanically treating and washing the MSW to recover two main fractions: recyclables and biomass. The washing stage generates a washwater containing soluble organic matter which can be a feed for high-rate anaerobic digesters to produce biogas, a source of renewable energy. The residual solid from washing is a 'clean' biomass rich in lignocellulosic fibre that can be converted into sugars via enzyme hydrolysis: these sugars form the building blocks for a wide range of products in a waste-based industrial biorefinery. The project will test novel methods including the use of specialised additives in the MSW washing stage to improve the quality of the washed cellulose fibre and increase its sugar yield, and a new low-cost agent for pH control, to reduce the risks of contamination from food waste and nutrients affecting the downstream sugar production stage.	

Round 4 Early Stage: Technical Feasibility Studies

Methods of Microbial Control in the Clostridial ABE Fermentation Process (MiCON) **Total Funding Awarded -** £106,482	
Challenge area – Commodity chemicals and materials	**Lead Investigator –** Liz Jenkinson, Green Biologics Ltd
Lead Co-I – N/A	**Project partner institutions/companies (names) –** N/A
Green Biologics is an industrial biotech company, currently re-commercialising the clostridial ABE fermentation process for the production of n-butanol and acetone from renewable and sustainable feedstocks. There are many challenges inherent in this commercialisation process, not just with the complexities of engineering and process design but also with ensuring the clostridial strains used exhibit robust phenotypes such as resistance to phage infections and ability to out compete microbes indigenous to the plant environment. This project aims to use an innovative and environmentally responsible alternative approach to the 'easy fix' solution of using antibiotics by instead taking advantage of bacteriocins: small peptides produced by a number of bacterial strains to destroy competing microbes in an environmental space.	

Enzyme co-localisation and aggregation for enhanced metabolic activity for commodity chemicals **Total Funding Awarded -** £187,394	
Challenge area – Commodity chemicals and materials	**Lead Investigator –** Jeremy Bartosiak-Jentys, ZuvaSyntha
Lead Co-I – N/A	**Project partner institutions/companies (names) –** University of Kent (Martin Warren)
Current approaches for enhancing bio-based commodity production are restricted to known biosynthetic pathways and limitations to metabolite toxicity. However, many key bio-commodities are made via aldehyde-intermediates such as acetaldehyde, lactaldehyde and propanaldehyde and their production is often limited because of the inherent toxicity of their chemical reactivity. Ways to reduce this toxicity would offer a significant advantage to the commercial production of these materials. This application outlines a major new strategy to reduce the toxicity of key metabolic intermediates such as acetaldehyde through the deployment of proteinaceous scaffolds. This approach will be coupled to a novel pathway that will be engineered in specific bacteria called acetogens that can live on gaseous exhaust fumes in order to produce a key chemical commodity called 1,3-butanediol.	

Round 4 Early Stage: Technical Feasibility Studies

Viable biotechnological production of industrial methacrylate polymers **Total Funding Awarded -** £154,158	
Challenge area – Commodity chemicals and materials	**Lead Investigator –** Reuben Carr, Ingenza
Lead Co-I – N/A	**Project partner institutions/companies (names) –** Lucite International
A global challenge is to improve the way in which mankind improves the consumption and disposal of commodity plastics. Alternative strategies to permit production of chemically identical “like-for-like” materials from sustainable biobased feedstocks as alternatives to existing petrochemical sources is required to help met the improve consumption and disposal of plastics. This application to Innovate UK is seeking to develop highly efficient routes to prepare polymethacrylates (i.e. Perspex) from non-fossil carbon based feedstocks. The project partners will build bespoke bacteria using state of the art synthetic biology methods to enable production of methacrylate intermediates. We shall recover and test the intermediates for their practical suitability in preparing and forming the plastics that Lucite sells to its existing customers.	

Novel enzyme diversity for improved cleaning and hygiene **Total Funding Awarded -** £162,445	
Challenge area – Processes to reduce cost or improve efficiency	**Lead Investigator –** Unilever
Lead Co-I – N/A	**Project partner institutions/companies (names) –** University of Exeter (Jennifer Littlechild, Mikhail Isupov)
Bio-inspired products / processes will have a major impact on the global society in 21st Century. The employment of biocatalysts in industrial processes is expected to boost a sustainable production of chemicals, materials and fuels from renewable resources. The scope of this proposal is to translate academic research into industrial applications by exploiting methods, techniques and databases to allow the identification and application of novel biocatalysts in biotechnological products and processes. Among the large spectrum of applications, we will translate the findings and apply the novel enzymes to the creation of new HPC products so that we can combat more efficiently and with better hygiene human sebum (body soil) contaminated garments and thereby reduce the environmental and economic costs of laundry.	

Round 4 Late Stage: Technical Feasibility Studies

Sugar replacement from microalgae **Total Funding Awarded -** £209,500	
Challenge area – Fine and speciality chemicals and natural products	**Lead Investigator –** Charles Bavington, GlycoMar Limited
Lead Co-I – N/A	**Project partner institutions/companies (names) –** Mars and MicroA AS
The project's goal is to provide a novel sugar replacement ingredient to the global food market. The ingredient is a specialist carbohydrate sustainably manufactured from a marine microalgae. The project will demonstrate new technology at industrial pilot scale to grow microalgae and purify the product from the microalgae cultures. The project brings together Glycomar Ltd (UK), an SME company specialising in the discovery and development of novel polysaccharide products, MicroA AS (Norway) an SME company specialising in technology for production of microalgae, and a market leading food company. These partners bring together the right skills to develop a game changing sugar replacement product, which will improve the health profile of confectionery and other foods.	

Late feasibility of novel methods for improved polyketide drug development **Total Funding Awarded -** £ 331,790	
Challenge area – Fine and speciality chemicals and natural products	**Lead Investigator –** Isomerase Therapeutics
Lead Co-I – N/A	**Project partner institutions/companies (names)** – John Innes Centre (Barrie Wilkinson)
Confirmation of scalability of new tools for accessing novel natural products with use in human and animal health and as agrochemicals.	

List of Collaborators

AB Agri	Acidophil
Algaecytes	Algenuity
AlgiPharma AS	Actavis Biologics (Now Allergan)
Arecor	Aston University
Avacta Analytical	Biocatalysts
Biome Technologies	Biorenewables Development Centre
Biosyntha	BioToolomics
Brocklesby	Carbosyntyh
CatSci	CelluComp
Centre for Environment, Fisheries and Aquaculture	CHAIN Biotechnology
Chirotech Technology	Cobra Biologics
CPI	Croda
C-Tech Innovation	Dextra
Ensus	EverGreen Gas
Fiberight	FMC Biopolymer
Food and Environment Research Agency	Fujifilm Diosynth Biotechnologies
Generon	GlycoMar Limited
GlycoSeLect	Glythera
Green Biologics	GSK
Heriot-Watt University	Horizon Discovery
Hypha Discovery Limited	Imperial College London
Ingenza	Institute of Food Research
Isomerase Therapeutics	ITM Power
James Hutton Institute	James Hutton Ltd
John Innes Centre	Kings College London
Knauf	Labgenius
LabXero	Lenzing
Limagrain UK	Lonza Biologics
Lucite International	Ludger
Marlow Foods	Mars Chocolate UK
MedImmune	Merck Sharp & Dohme
MicroA AS	Mylnefield Research Services
Newcastle University	National Institute for Biological Standards and Control (NIBSC)
NiTech Solutions Ltd	Northumbria University
Novozymes US	Open University
Oxford Genetics	PALL EUROPE LIMITED
Palm Paper	Perlemax
Plymouth Marine Labs	Prozomix
Puridify	Queen's University Belfast
Rebio Technologies	Rothamsted Research
Scottish Association for Marine Science (SAMS)	Sciex UK
Shasun Pharma Solutions	STFC - Laboratories
Stockton Israel	Suprafilt

List of Collaborators

Synthomer	The Crown Estate
Treatt Plc	UCB Celltech
Unilever	United Utilities
University College London	University of Aberdeen
University of Bath	University of Birmingham
University of Bristol	University of Cambridge
University of Dundee	University of East Anglia
University of Edinburgh	University of Exeter
University of Kent	University of Leeds
University of Liverpool	University of Manchester
University of Nottingham	University of Oxford
University of Plymouth	University of Reading
University of Sheffield	University of South Wales
University of Southampton	University of St Andrews
University of Strathclyde	University of Warwick
University of York	Velcourt
Vireol Bio-Industries	Vivergo Fuels
ZuvaSyntha	