

## Results of Competition: UK-China Collaboration to Tackle Antimicrobial Resistance

Competition Code: 1802\_CRD\_DH\_CHN\_AMR

Total available funding is £10,714,296

Note: These proposals have succeeded in the assessment stage of this competition. All are subject to grant offer and conditions being met.

Participant organisation names	Project title	Proposed project costs	Proposed project grant
Amalga Technologies Limited	Multifunctionalized Microalgae - A novel and flexible platform technology for maximising feed/energy conversion and treating severe infections in livestock	£189,841	£132,889
Moredun Research Institute		£68,011	£68,011
Plymouth Marine Laboratory		£186,525	£186,525
Rothamsted Research Limited		£319,787	£319,787
University of Exeter		£19,276	£19,276

Note: you can see all Innovate UK-funded projects here: <https://www.gov.uk/government/publications/innovate-uk-funded-projects>

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## Project description - provided by applicants

Production-purpose antibiotics are one of the great Faustian bargains of the modern era: mankind has traded increased livestock yields today for AMR tomorrow. We propose that microalgae can be readily engineered to express a wide range of naturally occurring antimicrobial and anti-inflammatory compounds which can both substitute for production-purpose antibiotics as a means of maximizing feed/energy conversion ratios and treat serious bacterial infections. Our objective in this project is to unequivocally demonstrate this using multi-functionalized microalgae (MM) modified to accumulate two such agents in a series of rigorous field-trials in both healthy and E.coli (K99)-infected calves. Our project is innovative in that MM can not only express these & numerous other functional biochemical compounds, but also constitute a uniquely low-cost and practicable platform technology. 350 million Chinese still live on less than \$3/day and microalgae is the only combined expression/delivery system capable of synthesizing the full range of bioactive agents required for managing the complexity of intestinal flora which can be cultivated by both industrial-scale and LMIC artisanal farmers alike.

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Arden Biotechnology Limited	Novel Biocontrol to Combat Clostridium Perfringens in Poultry Flocks	£809,471	£566,629
Avara Foods Limited		£49,630	£24,815
University of Lincoln		£158,410	£158,410

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## Project description - provided by applicants

This project is to develop a novel biocontrol ready for commercial sales to combat *Clostridium perfringens* (CP) in commercial poultry flocks. CP is the bacterium that causes Necrotic Enteritis (NE) in chickens. NE & subclinical NE are estimated to cost global poultry industry over \$6bn pa due to poor feed energy conversion levels, mortalities, vet & medicine costs and higher risk of human food poisoning. It is currently controlled by antibiotics which are under pressure to be withdrawn globally in the face of the global antibiotic crisis. This project's novel biocontrol will be a combinative narrow spectrum product specifically targeted against toxigenic strains of CP. It will act as a natural growth promoter (NGP) to be used in place of AGPs to support the global battle against AMR. Withdrawal of AGPs in animal husbandry must be combined with effective alternative NGPs to control NE if a catastrophic fall in feed energy conversion performance is to be avoided. This project will build on 5Yrs of research by the UK project lead including a 3 year KTP and now brings together a UK / Chinese consortium with diverse technical and commercial capabilities to successfully bring the product to market.

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Phoenix Medical Ltd	Adding Chinese herbal medicine to antibiotic treatment for acute exacerbation of chronic obstructive pulmonary disease	£239,848	£167,894
University of Southampton		£717,775	£574,191

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## Project description - provided by applicants

Over 25 million people in China had Chronic Obstructive Pulmonary Disease (COPD) in 2010, and this is projected to increase to over 42 million by 2020. Every year, the average COPD patient experiences 2-3 severe episodes called "acute exacerbations" (AECOPD). These are often caused by bacteria and treated with antibiotics, but many of these bacteria (especially in China) no longer respond to the commonest antibiotics, leading to prolonged hospital admissions and more deaths. Shufung Jiedu (SJ), a Traditional Chinese Medicine consisting of 8 traditional Chinese herbs, is already on the market in China. Preliminary research suggests that it can reduce risk of hospitalisation and duration of hospitalisation in patients with AECOPD, and so it could reduce the risk of antibiotic resistance. In this project we will conduct research in parallel in the UK and China to test the effect of SJ in tackling antibiotic resistance in AECOPD, both in laboratory models and in clinical trials. If successful, the results will support the inclusion of SJ in guidelines for the treatment for AECOPD both in China and in the UK, which will open up a very large market for the product.

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Participant organisation names	Project title	Proposed project costs	Proposed project grant
Epigem Limited	An integrated microfluidic – single cell Raman technology for rapid diagnosis of pathogens and their antibiotic resistance	£431,545	£302,082
University of Glasgow		£326,426	£326,426
University of Oxford		£120,000	£120,000

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## Project description - provided by applicants

The global spread of anti-microbial resistance (AMR) is one of the biggest threats to human health. A rapid diagnosis of AMR within 1-3 hours to infectious disease will not only reduce uncertainty in diagnosis, saving millions of lives (e.g. those lost through sepsis), but also enable an effective help to clinical doctors making the best use of antibiotics: preserving the usefulness of existing antibiotics for longer and reducing the urgency of discovering new ones. This project will develop such a diagnostic tool by integration of advances in single-cell Raman spectroscopy, microfluidics and lab-on-a-chip and world-leading clinical expertise. Our new methodology is based on the detection of the general metabolic activity of cells at the single cell level. It overcomes inherent limitations in the existing growth-based and DNA-based technologies, providing both speed and phenotype information needed for data-informed prescription. We anticipate that the implementation of this new diagnostic tool in healthcare will transform current approaches based on “empirical” rules, bringing significant benefits to patients and public health.

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The Vaccine Group Limited	Development of attenuated bovine herpesvirus-4 as a safe, inexpensive, single dose vaccine to control Streptococcus suis infection in domestic pigs	£576,334	£403,434
University of Plymouth		£294,350	£294,350

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## Project description - provided by applicants

Vaccines are one of medicine's greatest triumphs, having led to the virtual eradication of several deadly bacterial diseases. However, most vaccines in use today were developed by techniques pioneered over 100 years ago and do not represent the full potential of the field. Bovine herpes virus vaccines (BoHV-4) are one of the most promising classes of new vaccines, combining durability of immunity with low costs of manufacture. In this project, we will develop a novel BoHV-4 vaccine against *S. suis* - a major disease affecting pig farmers worldwide and a dangerous zoonotic pathogen in humans. The applicants will develop the novel vaccine using immunogenic *S. suis* proteins and then test it in pigs to convincingly demonstrate both efficacy and a quantifiable reduction in antibiotic usage. Our objectives are firstly to commercialize the vaccine within 3 years post-project and secondly establish it as a flagship product within our powerful BoHV-4 platform which can be targeted at many other serious bacterial infections affecting both animal and human health. The project is innovative in that there are currently no effective vaccines for the treatment and prevention of *S. suis* in pigs

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Participant organisation names	Project title	Proposed project costs	Proposed project grant
Nimrod Veterinary Products Limited	FARM WATCH: Fight AbR with Machine Learning and a Wide Array of sensing TeCHnologies	£327,081	£228,957
University of Nottingham		£514,249	£514,249

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## Project description - provided by applicants

Poultry is the 2nd most important source of meat in China, with consumption rapidly increasing. To meet demand, poultry production has made extensive use of antibiotics. China is the largest user of antibiotics for food production in the world (23%). Overuse of antibiotics has been accompanied by increased appearance of antibiotic resistance (ABR) and zoonotic transfer to humans via direct contact, environmental contamination and food consumption. Effective and rapid diagnostics of bacterial infection in chicken farming could reduce the need for antibiotics, thus reducing ABR. FARM WATCH will identify and validate new diagnostic biomarkers for use in the Chinese chicken farming industry. The biomarkers will be designed to predict and detect bacterial infection, resurgence of ABR, and zoonotic transfer to humans, by combining heterogeneous information collected from the production line. They will be developed from a thorough understanding of the epidemiological pathways of infection, from large-scale collection of data and statistical modelling / data mining powered by machine learning and cloud computing.

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Destiny Pharma PLC	Evaluation of novel XF Drugs as Bacterial Resistance Breakers	£517,706	£362,394
Cardiff University		£280,265	£280,265

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## Project description - provided by applicants

There is an urgent need for new drugs to treat infections resulting from bacteria that are now resistant to many of the current marketed antibiotics. This is a global issue encountered in low and middle-income countries (LMICs) where healthcare provisions may be less prevalent and so the impact is even greater. The jointly funded UK Department of Health and Social Care (DHSC) and Chinese Ministry of Science and Technology (MoST) Anti-Microbial Resistance (AMR) Industrial Research program aims to extend the knowledge surrounding the efficacy of novel anti-bacterial XF drugs to tackle World Health Organisation (WHO)-identified, high priority, multi-drug resistant (MDR) bacterial pathogens. The program will also examine the efficacy of these novel drugs in combination with existing, but largely ineffective antibiotics. Positive data from this study could lead to the development of a range of new medicines that could be competitively priced so as to permit patients from LMICs and China greater access to affordable medication.

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KPAD Ltd	Development of innovative premixes for pigs and poultry feed based on Chinese herbs for the replacement of extensively used antibiotics and hormones	£600,811	£420,568
University of Nottingham		£249,840	£249,840

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## Project description - provided by applicants

This project aims at the exploitation of bioactive compounds from Chinese herbs, in order to produce premixes for pigs and poultry feed, that can substitute for the antibiotics and hormones that are extensively used in livestock industries. The implementation of the project will solve the problem of the antimicrobial resistance that the irrational use of antibiotics and hormones in livestock is responsible for, while at the same time will propose environmentally friendly procedures and techniques for the extraction of bioactive compounds and the formulation of the feed premixes, contributing to the growth of livestock and the saturation of increasing demand. Moreover within the framework of the project a web platform and a database will be developed with information on the Chinese herbs and their functional properties, offering the chance and the knowledge to farmers to use alternative natural compounds.

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Biotangents Limited	Development of a shortlist-and-test diagnostic platform for brucellosis in livestock	£382,349	£267,644
Cranfield University		£266,946	£266,946
IceRobotics Ltd		£220,830	£154,581

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## Project description - provided by applicants

This project supports Biotangents (Penicuik), IceRobotics (Edinburgh) and Cranfield Univeristy in developing an advanced pen-side diagnostic test for brucellosis, a highly contagious bacterial infection that primarily affects livestock and poses an additional and significant threat to humans as a zoonotic disease. While Great Britain is officially brucellosis free, prevalence of the disease has been increasing in China in both animals and humans in recent years. Efficacy of antibiotics to treat brucellosis is variable. Biotangents will develop an accurate pen-side test to facilitate the identification of infected animals and allow the spread of the disease in livestock populations to be better controlled and the risk of transmission to humans, and subsequent demand for antibiotics for treatment, to be reduced. This will be tested in China alongside IceRobotics' behavioural monitoring platform that is able to monitor individual animal health status and shortlist those that may have acquired the disease.

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GAMA Healthcare Ltd	Encapsulated antimicrobial precursors for non-antibiotic treatment of MDRO in poultry	£115,823	£69,494
AGA Nanotech Ltd		£7,500	£5,250
CIELivestock Limited		£103,602	£103,602
Scotland's Rural College (SRUC)		£310,998	£310,998

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## Project description - provided by applicants

The use of antimicrobial treatments in agriculture is vital in protecting animal health and aiding the production of safe and nutritious food. However, previous overuse, and continued use of antibiotics in agriculture has been attributed to the rise in multi-drug resistance (MDR) bacteria, which can lead to ill-health and even death in humans if infected. MDR bacteria have been identified in large numbers of animals and raw food products, representing a major risk to public health and food system security. This is especially important in China and developing countries which rely heavily on animal products for nutrition and livelihoods, with chicken being the fastest growing protein source. GAMA Healthcare have developed an alternative antimicrobial treatment to conventional antibiotics by coupling a cancer medicine delivery system (microparticles) with a new class of short-lived antiseptic, which will be applied to reduce MDR bacteria in on chicken farms. The technology can be customised to meet the specific needs of the end-user, delivering a toxic payload to bacteria present within the animal and can be produced cheaply and safely, making it suitable for the agricultural/veterinary market.

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Oppilotech Ltd	Development of Key Technologies for Real-Time Diagnosis and Intervention of Resistant-Bacterial infections Based on Nanopore Sequencing.	£293,300	£205,310
Quadram Institute Bioscience		£436,765	£436,765

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## Project description - provided by applicants

The proposed project aims to tackle two of the major hurdles in the fight against AMR, new drugs and new diagnostics. The new diagnostics will utilise cutting edge UK technology (Oxford Nanopore sequencing) to provide test results with unprecedented depth of information within 6 hours as opposed to the current technologies which routinely take 24-48 hours. The approach to new drugs entails developing "Potentiators" - agents that can permeabilise the cell wall of bacteria allowing the use of established antibacterial compounds. The Potentiators in this project target Gram-negative (OPT-200) and Gram-positive (OPT-1) bacteria and both have novel modes of actions representing first-in-class antibacterial programmes. The focus of this project will be on Hospital Acquired Pneumonia (HAP) and subset of HAP Ventilator Acquired Pneumonia (VAP). HAP/VAP are important infections throughout the world and are a major cause of morbidity, mortality and increases in hospital stay resulting in escalation of healthcare costs. The long-term goals of this project are to provide rapid diagnosis technology for HAP/VAP that can be combined with a potentiator treatment regime.

Finance Summary Table – How to complete this section

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Oxford Vacmedix UK Ltd	Development of an early diagnostic system for CRE in a prospective ECMO cohort	£593,628	£350,000
Imperial College London		£375,562	£375,562

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Project description - provided by applicants

Awaiting Public Project Summary

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Molecular Warehouse Ltd	New Smart Diagnostics for Infection	£426,734	£298,714
University of Surrey		£455,435	£455,435

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## Project description - provided by applicants

Currently, diagnosing a bacterial infection and selecting the correct antibiotic treatment can take up to 48hrs and this often results in clinicians prescribing broad spectrum antibiotics, which may result in the development of antibiotic resistance. This project aims to develop rapid, accurate and economical diagnostic tests for use in China that will provide a diagnosis in less than 30 minutes without the need for complex laboratory equipment. Furthermore, the tests will provide important information on antibiotic resistance, therefore enabling the clinician to prescribe the most effective treatment and avoid the development of antibiotic resistance.

The project also aims to develop a Therapeutic Drug Monitoring (TDM) system that antibiotic treatments can be accurately monitored through a simple blood test. The TDM will ensure that patients receive the correct dosages of antibiotics for a given infection, thus ensuring rapid treatment of the infection and avoidance of antibiotic resistance. The project will also develop a knowledge-based platform will help physicians track infectious disease in China and provide advice to physicians on appropriate control strategies.

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Oxford Drug Design Limited	Novel small molecule and TCM approaches to support pig production, minimizing generation of resistance to human antibiotics	£805,788	£564,052
University of Portsmouth		£176,641	£176,641

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## Project description - provided by applicants

The emergence of resistance to antibiotics is a major health concern. To address this concern, this project will address multiple aspects of antibacterial resistance, bringing together complementary expertise in the UK and China. Antibiotics are widely used in agriculture, where they have a valid role in protecting farm animals from disease and increasing food production. However, the use of antibiotics that are also used to treat humans could lead to increased antimicrobial resistance. One of the aims of this project is to develop a new class of antibiotics that are specific to a species of bacteria that cause infections in pigs, which would enable reduced use of human antibiotics in farming. A second aspect of the proposal is to investigate the use of traditional Chinese medicines (TCMs) in veterinary settings. TCMs are typically complex mixtures with unknown mechanism of action. We will use sophisticated computational modelling methods, specifically a technique called chemgenomics, to identify the active components of TCMs, which may enable further classes of antibiotic to be rationally designed, or to be used synergistically with existing compounds.

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