Innovate UK

Results of Competition: Vaccines for Global Development – Preclinical
Competition Code: 1610_SBRI_DOH_PCDV

Total available funding is £10m

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
Imperial College London	EML-VAC: Multivalent replicon vaccine against Ebola, Marburg and Lassa viruses	£492,577	£492,577

Project description - provided by applicants
A multivalent hemorrhagic fever vaccine based on synthetic replicating ribonucleic acid (RepRNA) would provide one of the fastest and most cost-effective approaches to stop viral outbreaks at their source. This affords significant advantages over more conventional vaccine approaches such as viral vectors, and attenuated pathogens and would be safer in individuals unable to receive live attenuated vaccines (e.g. children and the immunocompromised). This vaccine may also find utility as a booster that can be used in combination with existing vaccines (e.g. rVSV-EBOV). The fully synthetic manufacture and ease of production provides the potential to produce hundreds of thousands of doses within a matter of weeks where the individual vaccine components targeting different hemorrhagic viruses can easily be combined. This may be critical to the global response against emerging hemorrhagic viral infections, as the nature of the next outbreak cannot be reliably predicted. In this respect the proposed multivalent vaccine has potential not only to protect against multiple known hemorrhagic viruses but is also more likely to show cross-protection against novel variants that may arise. The proposed vaccine can be effectively freeze-dried providing a portable and stable product that can withstand temperature oscillations without the requirement for a cold chain. The program aims to develop a multivalent vaccine against the most common human viral hemorrhagic fevers (two Ebola viruses, Marburg virus and Lassa virus). The choice of targets is based on strong scientific evidence that gene based approaches can protect against infection in preclinical models. This Part 1 project will support vaccine characterisation, proof of concept 'in vivo' studies and process finalisation, such that on completion of the project everything will be in place to rapidly move into early phase I human trials upon successful Part 2 funding. Our vision is to ensure appropriate costing for low and middle income countries and to make the vaccine readily available to organizations focused on global health (e.g. MSF and WHO), as these groups have historically been the first to detect, and/or respond to an outbreak, and are therefore ideally positioned to assist in implementing any vaccination strategy. Our Target Product Profile (TPP) is a temperature stable multivalent vaccine that can elicit protective immunity against the most common human viral hemorrhagic fevers following a single immunisation across all populations (adults, children and the immunocompromised), has potential for boosting in the absence of anti-vector immunity, and can be rapidly manufactured at low cost.

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Participant organisation names	Project title	Proposed project costs	Proposed project grant
Public Health England	Exploitation of x-ray irradiated viruses for vaccine development (XVacc)	£452,324	£452,324

Project description - provided by applicants
Many vaccines that have been successfully used for decades have relied on inactivating pathogenic material to render it uninfectious. One benefit of this approach will be the recipients immune system "seeing" the whole pathogen, so the resultant immunity generated will be primed in preparation for exposure to the live pathogen. Other benefits include immunity being generated across a wide array of antigens, rapid scalability, a known safety profile and cost effectiveness. Purified inactivated virus (PIV) vaccines were recently developed for Zika virus, demonstrating protection in animal models including non-human primates and are now entering human clinical trials with US government and commercial support. This work demonstrates that the application of PIV as vaccine candidates remains an important tool for producing rapid and efficacious interventions against pathogenic threats. To date, PIV vaccines are developed using chemical or radiological methods for inactivation; both of which confer severe disadvantages. Addition of inactivation chemicals, such as formaldehyde, risks altering the conformational structure of antigenic targets and compromising the recognition of protective epitopes. Harmful chemical used during the manufacture of vaccines will also need stringent removal before being used for clinical trials adding extra processing, costs and regulatory issues to vaccine development. Whilst gamma irradiation negates the need for chemical intervention, it has a severe limitation with the technology requiring radioactive isotopes for operation. This has financial, environmental, security and moral impacts associated with the use of radiation. X-ray irradiation offers a solution to the production of PIV vaccines by removing the need for radioactive sources to generate beams required to inactivate pathogens. This is a new and emerging technology with huge potential benefits, including being cheaper and secure for direct applications within developing countries. With the benefits of PIV vaccines being exemplified by the recently developed Zika virus vaccine, PHE would use Rift Valley Fever virus to develop a proof-of-concept approach for the use of x-ray irradiated material to generate vaccine candidates. If successful, this approach could be used across different viral pathogens and be highly relevant for responding to emerging health threats as can be rapidly applied to newly isolated viruses that might emerge and threaten human health.

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Participant organisation names	Project title	Proposed project costs	Proposed project grant
Excivion Ltd	A Novel Diagnostic for anti-Zika Antibodies to Inform Deployment of Zika Vaccines	£500,000	£500,000

Project description - provided by applicants
The Zika epidemic is a global problem with profound consequences for nations and families that will take decades to unfold. While there is an urgent need for a new vaccine against Zika, there is a similar urgency to accurately monitor, map and contain outbreaks of Zika (which is easily confused, symptom-wise, with other infections). Likewise it will be important to deploy precious vaccine resources effectively in the field in resource-limited countries, making sure the vaccine is deployed to 'current' outbreak-areas as a priority, as their geography changes over time, and saving health-care costs on unecessary use of vaccine. Also, it is important to monitor the effectiveness and safety of development/deployment of novel vaccines and to understand the risks of vaccine development against this 'new' virus, which is only one 'cog' in a rapidly evolving ecosystem of related viruses. Antibodies (resulting from prior infections with related viruses) already present in the blood of patients experiencing Zika virus infection may influence the course of the disease or the result of Zika vaccination (e.g. whether the naturally-encoutnered Zika virus crosses the placenta and damages the foetus, or whether vaccine strains might do the same thing), and antibodies generated by Zika vaccination may influence the occurrence of haemorrhagic fever upon encounter with dengue (a related virus that co-circulates with Zika). Current diagnostic practice is not adequate to properly enable the intelligent deployment of vaccines because it is based in central diagnostic labs that require the transport of blood samples from diverse, sometimes remote, areas of endemic countries, which is expensive and inefficient, and which may not be possible in many instances due to lack of the necessary refrigerated transport infrasctructure. What is needed to enable effective monitoring and safe development of Zika vaccines is a cheap 'point-of-care' diagnostic test, i.e. a test that can be run without the need for clean water, electricity or equipment - e.g. like a DIY pregnancy test, that can be operated in the home or in a Doctor's surgery. This is the subject of the current project. The new test will help define which subjects are eligible to receive Zika vaccination, maximising the safety and effectiveness of its deployment. It will also help define whether a subject has responded adequately to the vaccine (i.e. reached a 'to be determined' protective level of Zika-specific antibodies) or whether they may require a further dose (a factor that may vary in differing endemic territories, depending on prior exposure to related viruses). In order to deliver the test Excivion has fielded a world-class team of experts with the necessary skills in virology/immunology and in diagnostics development and evaluation in an endemic public-health setting. The project takes advantage of an unique set of viral proteins developed (by the applicant company) under SBRI funding which promise antibody-based diagnostics of unparalleled specificity (as well as safer vaccines).

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Participant organisation names	Project title	Proposed project costs	Proposed project grant
University of Oxford	Novel multivalent vaccines against haemorrhagic fevers	£483,455	£483,455

Project description - provided by applicants
Recent outbreaks of Ebola, MERS and Zika viruses have highlighted the lack of global preparedness and viable therapeutic solutions for known outbreak pathogens. To prepare for the control of future outbreaks, vaccine candidates against 'priority pathogens', as identified by the UK vaccines network and other organisations, should be taken forward into clinical development and tested for safety, immunogenicity and, wherever possible, efficacy. To be viable, new vaccine platforms will need to be 1) immunologically effective over time, 2) reliably deployable, and 3) cost effective. Monovalent vaccines, administered singularly against individual viruses, will be prohibitively expensive to develop for all ‘priority pathogens’ and burdensome to deploy in the prophylactic setting. Here, we propose to develop efficacious and cost-effective multivalent vaccines against several lethal haemorrhagic fever-causing viruses endemic in Africa, including Filoviruseses (Ebolaviruses & Marburg virus) and Arenaviruses (Lassa virus). Multivalent vaccines will allow the development and production outlays to be greatly reduced, and will increase the probability that vaccines against most, rather than a select few, pathogens will be available. Our pre-developed core vaccine platforms (viral vectors) have proven capability of expressing multiple antigens and inducing durable immune responses in other infectious disease settings. For each of the multivalent vaccines against outbreak pathogens that we develop, preclinical testing will be conducted to identify the vaccines which induce ‘best–in-class’ immune responses and are most suitable for clinical manufacture (GMP) and field use. By assessing several combinations of different antigens in two different viral vector platforms, we will optimise the chances of developing vaccination regimens suitable for both prophylactic and outbreak response settings. At the end of this work, we will have developed, tested and produced pre-GMP stocks as scalable vaccine solutions for deployment against Filoviruses and an Arenavirus and will have developed scalable platform modalities that can be used in other outbreak scenarios.

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Participant organisation names	Project title	Proposed project costs	Proposed project grant
University of Cambridge	Trivalent Lassa, Ebola and Marburg viral vaccine (Tri-LEMvac)	£695,639	£695,639

Project description - provided by applicants

African haemorrhagic fever viruses have a significant impact on human health in low income countries and developing economies (Heeney, J Internal Med, 2006). Lassa fever is endemic to Western Africa with estimates ranging between 300,000 to a million infections, with 5,000 deaths per year. It's overlapping geographic distribution with other Viral Haemorrhagic Fevers (VHFs) caused by Filoviruses such as Ebola virus (EBOV), complicated the early clinical diagnosis of Ebola virus disease in the 2014/2015 West African outbreak. A combined Old World Arenavirus and Filovirus vaccine eliciting protection against Lassa Fever virus (LASV), Ebola (EBOV) and Marburg (MARV) viruses, the most important haemorrhagic fevers in West and Central Africa, would be of great benefit in the control of spread of these notorious pathogens. Currently there are no licensed vaccines for these infections. A single vaccine to protect against all three of these regionally important VHFs that was economic, easy to produce, readily deployable and temperature stable in the absence of continuous cold chain storage would be highly desirable.
The Modified Vaccinia Ankara (MVA) vaccine platform is a non-replicating strain third generation smallpox vaccine and one of the most advanced recombinant poxviral vaccine vectors in human clinical trials (Cottingham & Carroll, Vaccine, 2013). MVA is a robust vector system capable of co-expressing up to four transgenes facilitating potent promoters and stable insertion sites (Orubu et al, Pone, 2012). We will bring synergistic new platform technologies together from EVAC and LassaVacc (Innovate UK). Using EVAC's DIOS synthetic immune optimised vaccine inserts to give the broadest possible vaccine protection, together with LassaVacc's MVA based LASV (NP/GPC T & B-cell antigens) we will develop a single trivalent vaccine (Tri-LEMvac) that will generate combined vaccine efficacy against future outbreaks of variants of the haemorrhagic fever Lassa, Ebola and Marburg viruses.

Towards this goal we propose two stages:
Stage 1) Proof of concept (this application). Within 12 months, we will demonstrate proof of concept by constructing trivalent MVAs expressing conserved Lassa, Ebola and Marburg antigen inserts in a single MVA, confirming optimal expression, demonstrating immunogenicity in small animals and efficacy by live virus challenges with these pathogens. MVA is a clinically trialled vaccine vector which we will use to compare improvements in immune responses, the breadth of protection, durability and efficacy. This new trivalent LEMvac MVA vaccine will allow direct comparison in head to head clinical trials in stage 2.
Stage 2) follow-up proposal; refine preclinical work, including GLP manufacturing toxicology/manufacturing. To perform first in human phase I trials of Tri-LEMvac to establish dose, durability of one shot versus prime boost and safety.

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Participant organisation names	Project title	Proposed project costs	Proposed project grant
Emergex Vaccines Holdings Limited	Validation and cGMP manufacture of a Zika and Multivalent Filovirus vaccine	£499,825	£499,825

Project description - provided by applicants
From mosquito borne viruses such as Zika, to human-to-human transmitted viruses such as Ebola, the risk of infectious disease remains a true medical challenge for the world. Developing countries are disproportionately affected; nearly all the victims in the recent Ebola epidemic lived in low income African countries while Zika continues to spread to the regions that do not have the resources available to deal with the lifelong disability associated with the foetal effects of infection. Such outbreaks occur rapidly and unexpectedly where a viable vaccine, the gold standard of defence against viral infectious disease, is not available. This highlights the urgent need for vaccines that can be developed quickly and on-demand and which are also affordable and practical in the low resource environments where they are required. Due to the high production costs, high manufacturing costs, requirement of cold and variable efficacy; existing vaccine technologies do not fit this need. Emergex has developed a novel synthetic vaccine platform technology, which it will apply to the generation of a vaccine against Zika and a multitarget vaccine against all strains of Ebola and Marburg . This involves the addition of viral components to a gold nanoparticle carrier system, resulting in ultra-small 100% synthetic vaccine agents. These synthetic vaccines that are highly stable, eliminating the need for cold chain and allowing an extensive shelf life. The synthetic nature also means the production process is fast, cheap and highly scalable: for our vaccines, we estimate that with current facilities 1 million doses could be produced in a day at cost of goods and manufacture of $0.109 per dose. This contrasts with the most advanced experimental Ebola vaccine, cAd3-EBO Z, an attenuated live vaccine generated in cell lines, which is estimated to have a production capacity of 100,000 to 500,000 doses over 9 months at a cost of $50-$250 per dose. With 70 million people in “at-risk” Ebola regions, where other technologies would fall short, the Emergex technology could provide an affordable and practical solution to meet the dose demand required to incur population immunity. The recent Zika outbreak can be defined as a foetal-maternal health issue. Evidence has confirmed a link between the Zika infections in pregnant mothers and birth defects (i.e. microcephaly ~ 1% incidence) of the foetus in utero. It is also now proposed that in 20% of cases maternal Zika can lead to some form of neurologic damage. This disproprotionately effects developing countres with limited resources to deal with lifelong disability. Since the mother cannot pass immunity to her child until late in pregnancy and there will always be a brief period where the foetus is exposed to infection, vaccination of the mother alone is not sufficient and vaccination of the feotus is required. The high safety profile and small size of our vaccines means we believe we are the only technology that is suited to in-utero vaccination The impact of infectious disease epidemics on emerging economies is enough to reverse or impede decades of development, meaning the effects reverberate for years to come. The importance of novel vaccine technologies that are suited to where and when they are needed has never been more evident

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Participant organisation names	Project title	Proposed project costs	Proposed project grant
Leaf Systems International Limited	Development of Virus-Like Particles as vaccines against emerging viral diseases	£490,375	£490,375

Project description - provided by applicants

Recent decades have seen changes in the mobility of arthropod vectors, driven by global warming. This has resulted in the spread of several diseases from their previously restricted ranges into larger naïve human and animal populations, resulting in severe epidemics. In addition, modern global transport networks has led to highly mobile human populations, who could transport a virulent infection around the globe within days. Recent outbreaks such as Zika and Ebola have highlighted this potential threat. To cope with new outbreaks, effective vaccines are required that are cheap to produce and can be deployed in regions of low technological sophistication and financial resources. However, the limited occurrence and geographic distribution of such diseases on a day-to-day basis have thus far precluded the development of such vaccines, on the basis of simple economics.

Many of the viral agents of these emerging diseases share common characteristics in their structures and lifecycles, notably the production of complex capsid and envelope structures that house the viral genomes. Virus-like particles (VLPs) are biological structures that comprise the outer shell of a virus but without the viral genome. In certain circumstances, VLPs can be produced in high quantities by expressing the structural components of a virus in a suitable host cell, where they can assemble into a form that closely mimics the native virus. Such VLPs can be highly immunogenic and very effective vaccines as they present all the antigenic components of the virus to the immune system, in a form that is identical to the real virus. Unlike killed or attenuated virus preparations, there is no risk of live virus contaminating the material or of genetic reversions giving rise to virulent virus de novo.

Many expression systems struggle to fold and assemble the viral proteins or to provide the required post-translational processing and maturation functions that are necessary to assemble a fully mature VLP. Even in expression systems where the processing is performed correctly, yields are often very low. Plant cells are highly competent at expressing, folding and assembling VLPs and often with high efficiency. This group have successfully produced VLPs of several significant pathogens, including Bluetongue virus and poliovirus. In the commercial sector, Medicago Inc. (Quebec, Canada) and Caliber Biotherapeutics (Austin, US) have been able to produce influenza VLPs, at scale, in very short timescales (12M doses in 30 days; 50M doses in 90 days, respectively) from genome sequence alone using transient plant expressions systems. Plant transient expression (PTE) facilities are reported to be less costly to build and operate than traditional fermentation or cell culture facilities, making them ideal to deploy in low-income economies or in quick-response, surge manufacturing situations.

This project aims to develop new VLP vaccine constructs from two of the most challenging viral targets that are considered a high-priority, namely Chikungunya virus (CHIKV) and Rift Valley Fever virus (RVFV). The construct(s) will be configured for PTE and the ultimate aim is to deliver VLP vaccine products, that are both inexpensive to manufacture and capable of rapid surge production.

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Participant organisation names	Project title	Proposed project costs	Proposed project grant
Plymouth University	Multivalent Attenuated Vaccine against Viral and Bacterial Zoonoses in Ruminants	£408,589	£408,589

Project description - provided by applicants

BACKGROUND: Infected animals and animal products are the most common route by which highly pathogenic microbes enter the human population. The list of these zoonotic (transmitted from animals to humans) microbes is extensive, but includes such viruses as Ebola and Lassa haemorrhagic viruses, SARS, MERS, and Rift Valley Fever virus (RVFV); and the bacterial causes of plague (Yersinia pestis) and Q fever (Coxiella burnetii, CB). The rate at which these microbes is entering the human population is on the increase, but unfortunately our ability to control their emergence remains severely limited. This problem is further complicated by the emergence of these microbes most commonly occurring in under-resourced, low-and middle-income countries (LMICs). The realization of this capacity gap underpins this current UK Vaccine Network Competition Brief.

APPROACH: Vaccination of animal populations involved in zoonotic transmission is one effective means of reducing pathogen emergence into the human population. The aim of the current project is to construct a single attenuated (reduced virulence*) multivalent vaccine targeting both RVFV and CB. It takes advantage of the near complete overlap of RVFV and CB in terms of their disease characteristics, including: i) animals they infect (ruminants: cattle, sheep, goats and camels), ii) geographic distribution, iii) at-risk human populations (farm and abbatoir workers, and veterinarians), iv) conditions under which they transmit zoonotically to humans, and v) symptomology both in humans and in animals (both microbes associated with abortion storms in goats and sheep). We will use bovine herpesvirus-4 (BoHV-4) as the platform for this vaccine, which has been shown to create an immune response in all common domestic ruminant animals tested. The BoHV-4-based vaccine will be attenuated by removal of a region of the virus called ORF73. Deletion of ORF73 results in the vaccine only being able to replicate for a transient, short period of time in animals. This further increases the safety of the vaccine, but does not affect its ability to induce a good immune response (this will also be confirmed during the 12 month project). Such attenuation is 'conditional' in that it prevents long-term replication in the animal, but does not affect ease/low cost of vaccine manufacture. A conditionally-attenuated BoHV-4 targeting both RVFV and CB is therefore suited for production and use in LMICs endemic for RVFV and Q fever. It will be safe, inexpensive to produce and able to create an immune response in the domestic ruminant animals involved in transmission of RVFV and CB to humans. It also has the potential for providing long-lasting immunity after only a single dose, further reducing vaccination costs. Finally, developing a vaccine for the animal populations involved in transmission, rather than for humans, considerably reduces the time to vaccine commercialization and use in the field due to the lower threshold of requirements for approval of animal compared to human vaccines. [*As even the wild-type version of BoHV-4 is not reproducibly associated with disease, deletion of ORF73 of BoHV-4 is included to provide an additional tier of safety].

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Participant organisation names	Project title	Proposed project costs	Proposed project grant
University of Oxford	Development of a novel vaccine to protect against Q fever epidemics	£469,049	£469,049

Project description - provided by applicants
The aim of this project is to create an innovative vaccine against Q fever, caused by the bacterium Coxiella burnetii. We propose to use a potent vaccine delivery technology, highly suited to outbreak situations in low-income countries, and never tried for this disease. Q fever is highly contagious, often transmitted to humans by infected livestock. It is a global health concern, classified a potential outbreak pathogens by the UK government, the CDC and WHO for several reasons: 1. It causes a range of disease from acute to potentially fatal chronic infection, and is particularly dangerous in pregnancy. 2. Extensive and costly antibiotic use may be required during outbreaks: while infections may be self-limited, antimicrobial therapy is effective in shortening illness duration and severity, but acute illness requires 14 days treatment. 3. Chronic Q fever is very difficult to treat, results in frequent relapses, causes severe symptoms and can be fatal despite treatment. 4. The symptoms are non-specific and thus Q fever is difficult to diagnose (there is no reliable diagnostic test). 5. Q fever has a worldwide distribution, particularly affecting low-income countries. The number of reported cases is likely an underestimation. In the US, around 3% of healthy adults, 10-20% of persons in high-risk occupations have been exposed. A large epidemic occurred recently in the Netherlands (2007 to 2010) that led to several deaths and long-term illnesses. 6. The bacterium is unusually resistant to drying and to heat, it can survive for years, and extremely low infectious doses (down to a single bacterium) are sufficient to cause infection. It is therefore also a potential bioweapon. The inactivated whole cell vaccine licenced in Australia induces severe adverse effects, requires pre-vaccination screening and thus is not suitable for extensive use, particularly in low-income countries and for outbreaks. The protective efficacy of conventional vaccines based on proteins in adjuvant is very limited, likely due to the weakness of this formulation in inducing the cellular immune responses that have been linked to resolution of Q fever infection. In this context, our proposed solution is to use viral vectors as a vaccine delivery platform. This technology is based on harmless replication-incompetent viruses, currently developed against numerous infectious diseases (Ebola, malaria, HIV…), but not yet investigated for Q fever. This technology is highly suitable when cellular immune responses are required for protection in addition to antibody responses, as it can induce both at remarkably high levels. This technology is suited to outbreaks in low-income countries: all vaccines developed for the recent Ebola outbreak were based on viral vectors. Importantly, this technology is perfectly suited to the challenge of antigen selection for Q fever vaccines: while the focus of the protective immune response is currently debated, the vectored technology allows the formulation and testing of multiple antigen targets and combinations, in a very short time frame, directly in the formulation that can progress to clinic. We will use Q fever proteins known to elicit immune responses and formulate them into our clinically relevant viral vaccine vectors. We will investigate the immune responses and levels of protection induced by the novel vaccines, and identify the most potent candidate. If successful, this project will provide a strong case for testing of this new Q fever vaccine in people.

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Participant organisation names	Project title	Proposed project costs	Proposed project grant
University of Edinburgh	A novel livestock vaccination platform to prevent zoonotic emerging infections	£327,239	£327,239

Project description - provided by applicants
Emerging and epidemic infections are frequently passed to humans through their interactions with livestock. Examples include infection with Coxiella burnetii (causing Q fever), Rift Valley Fever virus (RVFV) and Crimean Congo Haemorrhagic fever (CCHF) virus, each of which is sustained and sometimes amplified in animals. One approach to limit the risk of transmission is to vaccinate animals against infection, but this often involves the use of inactivated pathogens, which are expensive and difficult to produce and generate immune responses that are impossible to distinguish from natural infection. Vaccination can also be challenging in resource-poor settings, where effective veterinary management is lacking. Furthermore, emerging infections can evolve rapidly, such that the ability to reengineer or reformulate vaccines is necessary to retain their effectiveness. There is an urgent need for stable systems that can deliver multivalent antigens in cattle to limit human exposure. We have developed a novel, non-pathogenic protozoan parasite as a flexible and safe vaccine delivery vehicle that is well suited to deployment in low and middle income countries (LMIC). The parasite is the single-celled organism Trypanosoma theileri, which is found naturally in almost all cattle worldwide. This parasite can be easily and rapidly engineered to express heterologous antigens using existing modularised expression constructs that can be delivered systemically into recipients over a sustained period. Using an exemplar antigen from Babesia divergens (a cattle pathogen), we showed previously that vaccination using this system results in low-level prolonged immune stimulation to the delivered antigen at levels shown to generate protective immune responses to the target antigen. In the planned work, we will generate T. theileri lines expressing several antigens from the zoonotic threats, Coxiella, RVFV and CCHFV, and confirm their effective protein production using antibodies raised to recombinant proteins of each target. The vaccine vehicle will then be inoculated into cattle using T. theileri populations expressing one or more antigens (singly or in combination) and maintained over 12 weeks. Thereafter, immune responses generated to the expressed antigens will be measured to assess efficacy of immunisation in the context of single or multivalent delivery. We have shown previously that a single inoculation of the delivery vehicle is sufficient to establish and maintain persistence of the vehicle such that a ‘one-dose’ application suitable in LMIC is practical. The work here will demonstrate the potential for this flexible, sustained delivery system to protect cattle against emerging zoonotic infections, thus providing a barrier to epidemic outbreaks resulting from frequent human-animal contact in at-risk populations.

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Participant organisation names	Project title	Proposed project costs	Proposed project grant
Vaxinano	Nanoparticle-based Vaccine Platform against Zika Virus Infection	£208,500	£208,500

Project description - provided by applicants

Zika virus outbreak prompted the World Health Organization to declare this infection as a public health emergency. The infection is associated with fetal and neurological disorders and Zika vaccine must be developed. Zika belongs to the flavivirus family and to date, a few Zika vaccine candidates are under clinical trials but without concern about cost, stability in warm countries, large-scale production, feasibility or the administration route, especially in low and middle-income countries. Another evaded concern is the antibody-dependent enhancement of infection (ADE), a process aggravating the severity of co-infection by other flaviviruses when vaccinated.
Our project aims at developing new applications for our vaccine platform based on innovative nanoparticles (NPs) for which the proof-of-concept of the vaccine potential and efficacy has already been established. Our technology is safe, easy to produce at the industrial scale, it stabilizes the vaccine components even at high temperature (40°C), it is delivered via the nasal route and it elicits strong T-cell responses. The proposed target is the Zika virus and the strategy will use in parallel the inactivated virus and the recombinant antigenic DIII domain of the viral envelop to limit the ADE. The absence of antibody-enhanced infection by the vaccination will be evaluated against Dengue virus (DENV).
This project is the first step for the development of a technological vaccine platform against viruses to treat current and future viral outbreaks and unlimited perspectives are possible, starting with other flaviviruses like Dengue or Chikungunya viruses.

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Genefirst Ltd	Development of inducible expression-inactivated Leishmania as vaccine carries	£499,000	£499,000
Project description - provided by applicants			
Leishmania (protozoa parasite) has a number of inherent advantages, which make them favourable for serving as a universal vaccine carrier. Technology to produce transgenic Leishmania for expressing peptide vaccines is well-established. Its eukaryotic mechanisms of protein translation and post-translational modifications are used for overexpression of multiple vaccines episomally at high capacity. Leishmania can grow in defined media that is expandable to industrial scale cost-effectively. The surface coat of Leishmania has the unique properties of protecting vaccines and targeting, and thus concentrating them to the desirable immune cells to elicit effective immunity. Molecular overexpression-inactivation of Leishmania renders them completely non-viable, but substantially preserves the structural and functional integrity of their surface coat for safe and effective vaccine delivery.The efficacy of inactivated Leishmania as vaccines was shown by their ability to protect animals against experimental leishmaniasis. They were further shown to serve as an effective carrier to deliver a surrogate vaccine. The immune response was greater than that produced by the conventional means of delivery. High capacity of Leishmania transcription/translation makes this platform particularly attractive for expressing multiple transgenes as vaccines for immunotherapy against heterogeneous viral infections. In this project, we set up to develop a simple system of inducible overexpression-inactivated Leishmania as vaccine carriers for Ebola- Marburg-Lessa.			

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Innovate UK

Results of Competition: **Vaccines for Global Development – Preclinical**
Competition Code: **1610_SBRI_DOH_PCDV**

Total available funding is £10m

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
University of Oxford	Preclinical Crimean Congo Haemorraghic Fever Vaccine Development	£350,780	£350,780
Project description - provided by applicants			
Crimean Congo Haemorraghic Fever virus (CCHFv) is a severe haemorraghic tick-borne disease which causes outbreaks with a case fatality rate of 10-40%. Ticks infect livestock, mainly sheep although many species may be infected, and humans may be infected by tick bites or contact with infected animal body fluids after which human to human transmission may occur. The disease is endemic in Africa, the Balkans, the Middle East and parts of Asia and no vaccine is available for either humans or livestock. The Jenner Institute has developed the replication-deficient simian adenoviral vector platform ChAdOx1 to produce vaccines against a number of outbreak pathogens. ChAdOx1-vectored vaccines are highly immunogenic for both humoral and cell-mediated responses after a single dose, can be produced in a highly efficient manufacturing process and can be thermostabilised. Efficacy in livestock against Rift Valley Fever virus and safety in humans in a number of different vaccine programmes has been demonstrated. A ChAdOx1 CCHF vaccine has been produced and is immunogenic in mice. We now propose to conduct a more detailed immunogenicity study and then test vaccine efficacy of one and two dose vaccine regimens against lethal challenge in a mouse model. Data generated in this study will support an application for the next stage of the development process which will be to demonstrate vaccine immunogencity and efficacy in sheep in a CCHF-endemic area.			

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Innovate UK

Results of Competition: **Vaccines for Global Development – Preclinical**
Competition Code: **1610_SBRI_DOH_PCDV**

Total available funding is £10m

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
University of Strathclyde	New Application of a DNA-nanorod Platform for Vaccine Development	£394,466	£394,466

Project description - provided by applicants
In response to the call "Vaccine for Global Epidemics - Preclinical", we propose a new application of an existing novel DNA-nanorod platform for vaccine development against Lassa (LASV) and Nipah (NIV), two priority viruses. Although there are vaccines under construction against these two viruses (see Section 7), currently none are licenced. "We" are a consortium composed of teams from University of Strathclyde (UoS), Defense Science and Technology Laboratories (Dstl), and Touchlight Ltd London, a DNA technology specialist. The DNA-nanorod platform proposed here should elicit a broad T cell response as well as neutralising antibodies (nAbs), which are critical, in killing viral infected cells and in preventing viral invasion of host cells, respectively. These cellular and humoral immune responses are required for protection against LASV and NiV infection. As a proof of concept, the UoS team have shown that intranasal vaccination with gold nanorod (AuNR)-DNA, carrying a gene encoding the human papilloma virus (HPV) type 16 L1 capsid protein elicits immune responses in mice. The immune responses are characterised by high titres of nAbs and antibody seceting cells (ASCs) in spleens of vaccinated mice. We propose to exploit this DNA-AuNR platform in two ways to produce vaccines against LASV and NiV. For the NiV vaccine, we will clone the entire coding sequence of the viral glycoprotein (GP) to the mammalian expression vector, Luciferase-pcDNA3.1, under the CMV promoter. The NiV GP has been previously shown to elicit nAbs which recognise conformational epitopes on the viral surface and protect ferrets from an otherwise lethal dose of NiV (Pallister et al., Vaccine 2011. 29:5623). We will produce two vaccines for LASV on Luciferase-pcDNA3.1, by cloning the entire GP-coding sequence (LASV1) and by making an in frame gene fusion tween the 3'-end of HPV16L1 and 5'-end of the coding sequence of a LASV defined CD4 T cell epitope (LASV2). The HPV L1 protein spontaneously forms capsid and thus the chimeric construct will express the LASV CD4 T cell epitope on its surface to enhance the immunogenicity. All vaccines will be evaluated in mice via intranasal immunisation. The immune responses will be characterised initially by ELISA for total IgG and by ELISpot for ASCs using purified NiV and LASV GPs. Further evaluation will determine the potency and qualities of cellular and humoral responses by measuring levels of IgG1 and IgG2a, IFN-gamma and TNF-alpha producing CD8 and CD4 T cells, and memory T cells. The Dstl team will develop robust assays and growth methods for both viruses. These assays will be used for testing antisera from immunised mice for their capacity to inhibit LASV and NiV growth and/or plaque formation. If the vaccine candidates are shown to elicit a strong immune response, the Dstl team will take the lead to seek follow-on funding to evaluate the vaccine efficacy in appropriate animal models in vivo. Animal models may include guinea-pigs, ferrets or immune-deficient mice. Non-human primate models for either virus could also be developed if a smaller animal model shows promising results. Touchlight Ltd (London) will lead from TRL5 onwards for production of prototype vaccines.

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Innovate UK

Results of Competition: **Vaccines for Global Development – Preclinical**
Competition Code: **1610_SBRI_DOH_PCDV**

Total available funding is £10m

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
Public Health England	Multi-valent Hantvirus-Vaccine (MVA SEO-HTN: Vacc) and a ferret model of disease	£476,102	£476,102

Project description - provided by applicants
Seoul virus (SEOV) and Hantaan virus (HTNV) are widespread pathogens maintained in rodents and transmitted to humans in aerosols of rodent excreta. Human infection results in Haemorrhagic Fever with Renal Syndrome (HFRS), a key burden of disease in many low and middle income countries with between 100,000 –150,000 cases documented worldwide per year (1). HTNV and SEOV are members of the Hantavirus, a genus within the family Bunyaviridae comprising more than 20 viruses. The genus includes several other human pathogens such as Puumala virus (PUUV) and Dobrava virus (DOBV) which can also cause HFRS; then Sin Nombre virus (SINV) and Andres virus (ANDV) which cause a more infrequent type of disease, Hantavirus Pulmonary Syndrome (HPS), geographically restricted to the Americas (2). While the latter viruses are significant pathogens, the need for vaccine intervention against them is less urgent than for HTNV and SEOV (3). Significantly, SEOV is both globally widespread and has recently been determined (by this group) to be the cause of HFRS in the UK (4-5). Importantly the UK rodent reservoir includes wild rats, which have been responsible for SEOV transmission to farm workers (4) and pet rats which have been responsible for transmission to human owners (6). Trade in pet rats has also been responsible for the spread of the UK SEOV to Sweden (7) and the Netherlands (8) and there is evidence that this problem may be more widespread (9). The proposed multi-valent Hantavirus vaccine will be based on the vector Modified Vaccinia Ankara (MVA), which has a proven safety record and can elicit cellular and humoral immune responses to a wide range of antigens (10). MVA will be genetically modified to express the surface glycoprotein (GP) of SEOV and in tandem, a recombinant mosaic nuclear capsid protein (N) of SEOV and HTNV. We have good experience of the construction and development of recombinant MVA vaccines based on other Bunyaviruses (11), thus we expect this new multi-valent Hantavirus vaccine to result in the induction of an appropriate humoral and cellular immune response which will be assessed prior to protection studies in vivo work in an animal model. In order to establish protection studies we will conduct immunization and virus challenge experiments in a new animal model of HFRS disease. Currently there are NO small adult animal models that replicate HFRS disease in the background of a fully adaptive immune system, despite several studies (12). Significantly however, ferrets have not been assessed. Nevertheless, they have proven to be particularly useful in modelling a range of diverse human diseases such as those caused by Human Respiratory Syncytial virus (HRSV) (13), Nipah virus (14) and Ebola virus (15) which are often refractory in other animal species. Thus we will undertake in parallel to the vaccine construction, the development of a HFRS disease model in the ferret. While high-risk, the successful reproduction of disease in vivo would revolutionise Hantavirus translational research and enable proof of concept for this new Hantavirus vaccine. platform.

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Innovate UK

Results of Competition: **Vaccines for Global Development – Preclinical**
Competition Code: **1610_SBRI_DOH_PCDV**

Total available funding is £10m

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Participant organisation names	Project title	Proposed project costs	Proposed project grant
University of Oxford	Pan-filovirus T-cell Vaccine Designed as Bi-valent Conserved Region Epigraphs	£499,155	£499,155

Project description - provided by applicants
Since their discovery in 1967, viruses in the Filoviridae family have caused over 50 outbreaks, of which the last one was the devastating epidemic in West Africa during 2013-16. They cause hemorrhagic fevers in humans and non-human primates with 90% fatality rates and there is no licensed drug or vaccine. This family includes 5 distinct species in the Ebolavirus genus: Ebola (EBOV), Sudan (SUDV), Reston (RESTV), Tai Forest (TAFV), and Bundibugyo (BDBV) viruses; 2 viruses in the Marburg-virus genus: Marburg (MARV) and Ravn (RAVV) viruses; and 1 virus species in the Cuevavirus genus: Lloviu virus (LLOV). To date, most vaccine efforts focus on induction of neutralizing antibodies against EBOV, and also SUDV or MARV. While there is a high degree of conservation within one species, so that, for example, antibody responses to EBOV vaccine would likely cross-react with other EBOV outbreaks, protection against other filoviruses will be very low. Furthermore, future outbreaks may result not only from re-emergence of a virus of a rare species, but also of a completely new, as yet unencountered species. We have designed a vaccine designated FILOcepX with the aim to protect against all filoviruses (Theiler et al. Sci Rep 2016, 6:33987). Our vaccine focuses on induction of effective killer T cells targeting the 4 most conserved protein regions among the entire known Filoviridae family. Because there is a remaining diversity even within conserved regions, the vaccine optimizes the match to all known species by employing computed bi-valent epigraphs (a pair of proteins) used as the vaccine immunogens (cep for Conserved EPigraphs). The two epigraphs complement each other, are always used together and are delivered by safe common cold-like adenovirus and smallpox-like vaccines in a simple, in humans proven highly immunogenic regimen. The T-cell strategy is supported by published protection of macaques against challenge with homologous EBOV challenge through vaccine-induced killer T cells. In preliminary experiments in two strains of mice, research-grade FILOcepX vaccines induced killer T cells recognizing many virus regions. Achieving the aims of Stage I will demonstrate the technical feasibility of our solution, provide a proof-of-concept protection against 2 distant viruses EBOV and MARV in macaques and indicate correlates of T-cell protection for future confirmation to inform licensure, and prepare vaccines for manufacture for human use. If invited, Stage II of the Innovate UK will evaluate the vaccine safety and immunogenicity in a small phase 1 clinical trial in Oxford adults. Post Innovate UK, strong and broad im-munogenicity in humans supported by protection against two viruses in macaques may lead to a phase 2 trial in most at-risk human populations. Since phase 3 efficacy trial is not likely to be feasible, licensure may proceed through alter-native regulatory pathway based on macaque correlates of protection and human phase 2a safety and immunogeni-city. Licenced vaccine would have multiple uses ranging from generation of vaccine stockpiles for containment of future outbreaks, elimination of the 2013 outbreak remnants, provision of long-term protection in high-risk popula-tions to saving highly endangered western gorillas. Potential funders would involve international development agen-cies, the World Bank, philanthropies, defense funds, national governments in risk countries or large vaccine Pharmas.

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Results of Competition: **Vaccines for Global Development – Preclinical**
Competition Code: **1610_SBRI_DOH_PCDV**

Total available funding is £10m

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Participant organisation names	Project title	Proposed project costs	Proposed project grant
Agri-Food and Biosciences Institute	Development of a Novel Nipah Virus Pre-Fusion Protein Recombinant Vaccine	£271,373	£271,373

Project description - provided by applicants
Nipah virus (NiV) is a member of the Henipavirus genus (family Paramyxoviridae) and is the causative agent of sporadic outbreaks of respiratory and encephalitic disease in Southeast Asia. During the initial NiV outbreaks in Malaysia and Singapore, most human NiV cases were caused by close contact with pigs. In subsequent outbreaks during 2001 to 2012 in Bangladesh and India, drinking fresh date palm sap, which was contaminated by fruit bat's droppings, urine and saliva, and close contact with infected humans were found to be the major source of NiV infection. However, pigs are highly susceptible to NiV and generally serve as an amplifying host of the virus. Due to the lethal nature of disease and potential risk of reversion of a live attenuated vaccine to wild-type is not advisable. Therefore, many candidate vaccine for NiV are 'recombinant', where NiV proteins are produced from inserted genes in another safer virus (referred to as the vector). The fusion (F) and (G) proteins of NiV are commonly chosen as they provide an effective immune response in the body. The G protein allows the virus to attach to the cell and the F protein causes fusion of the virus envelope with the cell membrane so that the virus nucelic acid can enter the cell. Recently it has been discovered for several other paramyxovirus that the form of the F protein in the mature virus (post fusion form) is not as good at inducing an immune response as the form of F which occurs when the virus is entering cells (pre-fusion form). The pre-fusion F protein is unstable but we are able to stabilise this by making slight sequence changes. We will use another 'safe' member of the Paramyxovirdae, Sendai virus (SeV, a rodent virus) as the vector. We will compare the immune response of the SeV vaccines which produce one of the 2 types of F protein alone or each in combination with the G protein. Increasing evidence indicates that SeV has substantial potential as a vaccine vector in part because the virus uses common sialic acid receptors for cell entry, which facilitates infection of a wide range of cell types from different species including pigs and humans. Although SeV biosafety risks are minimal, we will also develop the system to generate replication-incompetent SeV NiV vaccines that infect host cells and produce the NiV F and G proteins but removes any residual biosafety concerns of a live SeV vector spreading between animals or humans. We hypothesise that novel vaccine approach based on replication-competent and incompetent SeV vectors expressing pre-fusion NiV F protein will provide a significant breakthrough in the generation of highly successful NiV vaccines. We further hypothesise that NiV vaccines based on rSeV expressing pre-fusion NiV F will induce more robust and longer lasting protective immunity than post fusion F vaccines. Used as a pig vaccine these systems will greatly reduce porcine to human transmission. Futhermore, production of non-replicating SeV vaccines addresses biosafety. As Sev also infects human cells, these vaccines could be subsequently trialled for human use.

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Participant organisation names	Project title	Proposed project costs	Proposed project grant
Activirosomes UK Limited	Preclinical PoC of Multivalent Vaccine Agents & Technology Platform	£448,950	£448,950

Project description - provided by applicants
PRECLINICAL PROOF OF CONCEPT OF SAFE, EASY TO FORMULATE AND ECONOMICAL MULTIVALENT VACCINE AGENTS FOR EBOLA, CHIKUNGUNYA AND ZIKA USING THE ACTIVE VIROSOME VACCINE DEVELOPMENT PLATFORM TECHNOLOGY. This project demonstrates pre-clinical proof of “Active Virosome Vaccines” for prevention of Chikungunya, Zika and Ebola virus infections. It will not only produce new, inherently safe, low cost and easy to produce vaccine agents for prevention of these infections and so suitable for responding quickly to outbreaks of these and other viral diseases, including in the countries where they are endemic. The project uses the "Active Virosome" technology platform, which is a simple, safe and efficient biotechnology for producing candidate vaccines, and can be easily modified to produce vaccines for new viral infection outbreaks, simply by slotting in a suitable "cassette" of genetic information. ActiVirosomes UK Limited, a young UK based biotechnology company, leads the project. The project lasts one year and costs £448,950. It will demonstrate pre-clinical proof of concept of up to 3 candidate vaccines for single viral diseases and two candidate vaccines designed to give protection against more than one viral disease at once: the candidate vaccines will continue through development and safety testing from April 2018 and could start clinical trials in humans as soon as 2020. Active Virosomes have many advantages compared to other vaccines against viral infections, including their safety and low cost of development and manufacture, which makes them particularly suitable for development and use in low and middle income countries which suffer from viral infections carried by mosquitos.

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Competition Code: **1610_SBRI_DOH_PCDV**

Total available funding is £10m

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Participant organisation names	Project title	Proposed project costs	Proposed project grant
University of East Anglia	Using engineered gut bacteria-derived microvesicles for plague vaccines	£499,798	£499,798

Project description - provided by applicants
There is currently no licensed plague vaccine in the Western world. We have developed a novel drug delivery technology platform that exploits the natural production of nanoscale microvesicles called outer membrane vesicles (OMVs) by bacteria residing in the human gut. These OMVs are highly stable and possess an unyielding outer membrane that protects their cargo from degradative enzymes and the hostile environment of the gut. We have previously shown that gut bacteria use OMVs to transfer and deliver proteins to cells lining the gut to influence their behaviour and function. Of particular interest to this application is the observation that OMVs can access and deliver proteins to specialised antigen presenting cells (dendritic cells) that key to initiating immune responses and in particular, generating antibody producing B lymphocytes. These properties make OMV attractive candidates for the delivery of agents, including vaccines, to the gut and other mucosal tissues. We have therefore developed the capability of engineering OMV-producing gut bacteria to incorporate vaccine antigens in their OMVs for delivery via the oral and nasal route. This overcomes the need for needles and provides immunity to infections in the lungs and gut that are the major routes by which the plague bacterium gains entry to the body and for which current plague vaccines are largely ineffective. In this application we will deploy our OMV-based drug delivery technology to develop new plague vaccines that protect against both bubonic and pneumonic plague infection. The use of OMVs from Neisseria meningitides and Vibrio cholera in licensed vaccines for protection against meningitis and cholera respectively, represents proof-of-concept for both the use of OMVs as vaccines and as a trailblazing product for the manufacturing/purification technology. The key objectives of this Stage 1 application are to determine the suitability of an OMV based vaccine produced by a commensal gut bacterium expressing in their OMVs the plague antigens F1 and V that are associated with protection agianst natural infection. This will be achieved through: 1. Platform Development; by optimising OMV-antigen formulation and dosing regimens using experimental models that faithfully reproduce human plague infection and vaccine responses, and assay development to investigate mechanism of immune protection. 2. Risk Reduction; by determining the impact of OMV-vaccine formulations on indigenous bacterial populations in the gut, and by demonstrating the absence of any vaccine reactogenicity and inflammation at sites of administration. 3. Delivery and Functionality in vivo; by determining the experimental model best suited for the study, and the optimal OMV delivery route(s) that generates the highest levels of vaccine antigen-specific antibodies in the lungs and gut (IgA) and in the blood (IgG). The final output will be a robustly tested platform technology for the delivery of plague vaccines to provide front line protection against the major forms of plague infection that will be suitable for assessing parameters of protective immunity (strength, specificity and duration), and vaccine protection testing in a Stage 2 study.

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Participant organisation names	Project title	Proposed project costs	Proposed project grant
Liverpool School of Tropical Medicine	Adjuvant free vaccines and companion diagnostics to control emerging flaviviruses	£382,974	£382,974

Project description - provided by applicants
We developed, patented, and licensed to UCB Pharma a platform technology that allows for multimerisation of the IgG-Fc into nanoscopic virus-like structures that are able to cross-link immune receptors found on antigen presenting cells with high specificity and avidity (Fig. 1). Here we wish to determine if this technology can be repurposed for the delivery of flaviviral antigens directly to antigen presenting cells, to develop novel vaccines, not only against Zika, but also other flaviviruses. The last 20 years have seen the emergence of two flaviviruses as major disease threats - West Nile Virus and Zika virus. There are currently no human vaccines available for diseases due to either of these viruses. Our approach may provide a platform for the rapid development of new vaccines for the emerging flaviviruses of the future - there are at least 30 other flaviviruses that can infect humans. In addition, our approach may dispense with the need for adjuvants by mimicking the natural immune-potentiating effects of immune-complexes (ICs). We shall use related model antigens from Zika virus (ZIKV) and other flaviviruses (one from each flavivirus group) to test the feasibility of this technology. A useful by-product of this application may be improved diagnostics that discriminate between emerging flaviviruses with greater sensitivity and selectivity. Indeed, the pseudo virus-like scaffold may also have therapeutic utility in the removal of antibodies that enhance disease. If we can show proof-of-principle with model flavivirus antigens, our technology should also be applicable to any of the diseases in the call, as well as having other applications. For example, any of the nine Fc-fusions drugs with FDA approval may be converted from monomers to multimers, thereby creating molecules that can bind more disease-causing ligand. Some of the potential benefits and applications of our patented platform technology are discussed in Czajkowsky et al, EMBO Mol Med 2012,4:1015-28 . If this proposal is successful, the potential added value in the development of new drugs, diagnostics and vaccines is very large.

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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
National Institute for Biological Standards & Control	Serological Vaccine Standards for Ebola, Zika and MersCoV	£499,995	£499,995

Project description - provided by applicants
The development of safe, effective and economically affordable vaccines against Ebola virus, Zika virus and Middle East respiratory syndrome coronavirus (MersCoV) would not only provide powerful tools for preventing re-emergence of these diseases in countries where they are endemic, but also enable swift and effective controls of outbreaks as a result of re-patriated infections in the UK. However, because these infectious agents can only be handled under high levels of biosecurity, the cost of working on these agents is prohibitive for most commercial organisations. The availability of established standards and reference materials accelerates the development of licenced vaccines. Where there is robust evidence that convalescent sera (serum obtained from someone who has recovered from an infectious disease) protect against reinfection, then the preparation and distribution of serum standards that have been demonstrated to confer protection against infection is hugely beneficial. It facilitates pre-clinical and early clinical development and selection of the most promising experimental vaccines without the need for expensive studies under biocontainment, as the serum standard provides an in vitro reference marker for serological protection. NIBSC is the global leader in the development of World Health Organisation (WHO) established International Standards and reference materials for biological medicines such as vaccines. At the request of the WHO, NIBSC has embarked on a programme of developing and establishing sero-diagnostic reference materials for the WHO's priority list of pathogens that heavily overlaps with the UK Vaccine Network's Priority Pathogen list. An International Reference Reagent for anti-Ebola virus antibodies has been established by the WHO's Expert Committee for Biological Standardisation and candidate standards for anti-Zika virus and anti-MersCoV antibodies are in advanced preparation. Although international, multi-laboratory analyses of these antiserum standards provides detailed information about their performance in in vitro assays, it is not possible to undertake the relevant in vivo protection studies because of the prohibitive cost to access suitable high containment facilities. NIBSC is collaborating with the Defence Science and Technology Laboratory (Dstl) and Public Health England (PHE) laboratories in Porton Down that have high level bio-containment facilities, to establish the in vivo protective titre of the established and candidate serum standards for Ebola virus, Zika virus and MersCoV. Using established models of infection at each centre, an accelerated programme of protection studies for all three reference standards will be completed within 12 months. This is the first step in the ongoing programme to establish serological diagnostic and vaccine standards for the 12 high priority pathogens identified by the UK Vaccine Network.

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