2nd Call for Proposals
Innovative Medicines Initiative 2

Version: FINAL

Innovative Medicines Initiative 2
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INTRODUCTION

The Innovative Medicines Initiative 2 (IMI2) Joint Undertaking has been created[1] following the below principles:

- Research related to the future of medicine should be undertaken in areas where societal, public health and biomedical industry competitiveness goals are aligned and require the pooling of resources and greater collaboration between the public and private sectors, with the involvement of small and medium-sized enterprises (SMEs).
- The scope of the initiative should be expanded to all areas of life science research and innovation.
- The areas should be of public health interest, as identified by the World Health Organisation report on priority medicines for Europe and the World (2013 update: http://www.who.int/medicines/areas/priority_medicines/en/).

The initiative should therefore seek to involve a broader range of partners, including mid-caps[2], from different sectors e.g. biomedical imaging, medical information technology, diagnostic and/or animal health industries (while ensuring gender matters are considered). Involving the wider community in this way should help to advance the development of new approaches and technologies for the prevention, diagnosis and treatment of diseases with high impact on public health.

The IMI2 Strategic Research Agenda (SRA) is the main reference for the implementation of research priorities for IMI2. Based on the SRA the 2014 scientific priorities for IMI2 have been prepared, which include a theme on infectious diseases which is addressed in this call.

Applicant consortia are invited to submit proposals to one of the topics. These proposals should address all aspects of the topic to which the applicant consortia are applying. The size and composition of each consortium should be adapted to the scientific goals and the expected key deliverables.

While preparing their proposals, applicant consortia should consider the participation of any legal entities carrying out activities relevant for the topic objective[3] and ensure that needs of patients are adequately addressed and, where appropriate, patient involvement is encouraged. Synergies and complementarities with other national and international projects and initiatives are expected in order to avoid duplication of efforts and to create synergies on the global level and to maximise European added value in health research. Where appropriate, the involvement of regulators is also strongly encouraged.

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1 The Council Regulation (EU) No 557/2014 of 6 May 2014 establishing the Innovative Medicines Initiative 2 Joint Undertaking.

2 Under the IMI2 JU, mid-sized companies having an annual turnover of EUR 500 million or less, established in a EU Member State or an associated country, are eligible for funding.

3 See the list of countries and applicable rules for funding under H2020:

http://ec.europa.eu/research/participants/data/ref/h2020/wp/2014_2015/annexes/h2020-wp1415-annex-a-countries-rules_en.pdf

Before submitting a proposal, applicant consortia should familiarise themselves with all call documents such as the IMI2 Manual for evaluation, submission and grant award, and the IMI2 evaluation criteria.

DISSEMINATION AND DATA STANDARDS

The successful applicant consortium will be expected to adhere to the following principles, if inappropriate please provide rationale.

1) Disseminate scientific publications and research data on the basis of open access. Collection, processing and generation of research data is to follow documented data management procedures (see "Guidelines on Open Access to Scientific Publications and Research Data in Horizon 2020" and "Guidelines on Data Management in Horizon 2020"). In order to ensure adherence to the legislation concerning protection of personal data, controlled access digital repositories and data governance will need to be established.
2) IMI2 projects should use well-established data format and content standards in order to ensure interoperability to quality standards. Preferably, existing standards should be adopted. Should no such standards exist, consideration should be given to adapt or develop novel standards in collaboration with a data standards organisation (e.g. CDISC).

IMI2 EBOLA AND OTHER FILOVIRAL HAEMORRHAGIC FEVERS PROGRAMME

BACKGROUND AND PROBLEM STATEMENT

Filoviruses is a family of viruses of which the most commonly known members are Ebola virus and Marburg virus. Both viruses cause severe, usually lethal haemorrhagic fever in humans and non-human primates (monkeys, gorillas and chimpanzees). Filoviruses differ from dengue and other haemorrhagic fevers due to the fact that they can spread directly from person to person, where many other haemorrhagic fevers require an intermediate host, like a mosquito, to spread the disease. Ebola virus disease (EVD), previously known as Ebola haemorrhagic fever, is a rare and deadly disease caused by infection with one of the Ebola virus strains. It has an incubation period of 2-21 days, and it usually begins as a sudden influenza-like syndrome, which rapidly progresses to multi-organ failure and coagulation abnormalities which manifest as internal and external haemorrhages.

The virus is transmitted to people from wild animals and spreads in the human population through human-to-human transmission via bodily fluids. Because Ebola virus is spread through contact with the body fluids of symptomatic patients, transmission can be stopped by a combination of early diagnosis, contact tracing, patient isolation and care, infection control, and safe burial. Before the current epidemic in West Africa, outbreaks of Ebola in central Africa had been limited in size and geographic spread, typically affecting one to a few hundred persons, mostly in remote forested areas.

The current outbreak in West Africa is due to the Zaire Ebola virus, a strain that historically has been the cause behind most EVD-related deaths.

The World Health Organization (WHO) was notified on March 23, 2014, of an outbreak of EVD in Guinea. The disease soon spread to the bordering countries of Liberia and Sierra Leone, which are the most severely affected countries. On August 8, 2014, the epidemic was declared a “public health emergency of international concern” (ref WHO Ebola Response Team, NEJM 2014, 371, 1481). Suspected cases of EVD have since been reported in seven affected countries (Guinea, Liberia, Nigeria, Senegal, Sierra Leone, Spain, and the United States of America).

Unprecedented in scale and geographical distribution since the identification of Ebola in 1976, the current epidemic has an apparent overall case-fatality ratio of about 70%; but it is suspected that many more cases have gone unrecorded. The WHO reported on October 14, 2014 that the number of new Ebola cases could reach 10,000 per week by December 2014. On October 31, more than 4.900 deaths and 13.567 cases had been reported in Sierra Leone, Liberia and Guinea, according to the WHO.

While there is no licensed treatment yet available for EVD, a range of blood, immunological and drug therapies are under development and two potential vaccine candidates are undergoing

evaluation, according to the WHO (http://www.who.int/mediacentre/news/statements/2014/ebola-therapies-consultation/en/).

NEED AND OPPORTUNITY FOR PUBLIC-PRIVATE COLLABORATIVE RESEARCH

The European Union is currently funding research addressing Ebola under the EU's Seventh Framework Programme (FP7) for Research and Development: on the development of new antiviral drugs and vaccines, on linking up high-security laboratories, on the clinical management of patients particularly in Europe, and on solutions to ethical, administrative, regulatory and logistical bottlenecks that prevent a rapid research response. Due to the emergency situation caused by the current outbreak of EVD, the European Commission has also recently mobilized a total of EUR 24.4 million (EU financial contribution) under Horizon 2020 through a fast-track exceptional procedure. As a result, five projects were selected for funding; these projects include a phase II trial of the GSK vaccine candidate ChAd3-EBOV (EU financial contribution EUR 15.1 million) as well as clinical trials on compounds (Favipiravir) and passive immunotherapy (convalescent plasma and horse serum). Also included is a project conducting translational research to provide answers to relevant clinical questions.

In view of the current epidemic, several other major public and private funders are engaging into funding urgent Ebola research. Main funders include the U.S. National Institutes of Health and the Bill and Melinda Gates Foundation in the US, the Department of International Development (DFID) and The Wellcome Trust in the UK, as well as individual EU member states like France and Belgium.

However, a programmatic approach addressing different challenges across the entire innovation cycle and leveraging input and multidisciplinary expertise across stakeholders is needed. IMI2 offers a unique opportunity to complement the ongoing European and international efforts by offering a multi-company, cross-sector and multi-stakeholder programmatic approach to address the challenges of EVD and other filoviral haemorrhagic fevers.

CALL TOPICS

The topics of the proposed IMI2 Ebola and other filoviral haemorrhagic fevers programme (the Ebola+ programme) cover actions that will address short term challenges of the current epidemic as well as actions needed to address EVD and other filoviral haemorrhagic fevers in a sustainable way for the long-term (see also conclusions from the high level WHO meeting on Ebola Vaccines Access and Financing of 23 October 2014[4]). To address the present challenges of the ongoing epidemic, the following topics are launched in the current Call for proposals in a fast track single-stage procedure:

4 http://www.who.int/mediacentre/news/ebola/23-october-2014/en/

IMI2-2014-02-01	**Vaccine development Phase I, II, and III**
IMI2-2014-02-02	**Manufacturing capability**
IMI2-2014-02-03	**Stability of vaccines during transport and storage**
IMI2-2014-02-04	**Deployment and compliance of vaccination regimens**
IMI2-2014-02-05	**Rapid diagnostic tests**

Additional topics under the Ebola+ programme may be launched at a later point and may cover the following areas:

- Immunotherapy
- Formulations for cold chain
- Rapid diagnostic tests – long term
- Antivirals development and repurposing
- Multivalent filovirus vaccine development

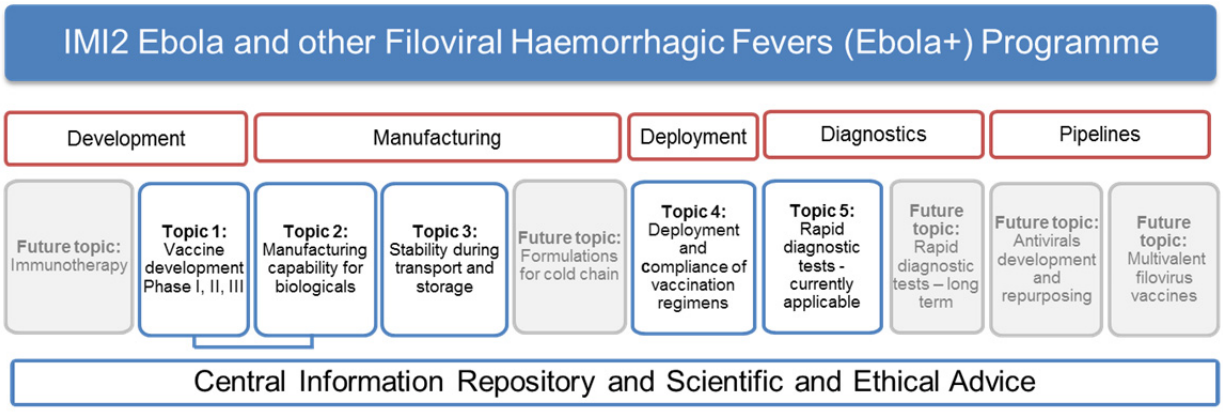

Figure 1: Proposed structure of the IMI2 Ebola and other filoviral haemorrhagic fevers (Ebola+) programme. Topics addressed in the current Call for proposals are highlighted in blue boxes. Potential future topics to be launched at a later point are shaded in grey.

All consortia participating in projects funded under the programme should closely interact and collaborate to ensure that learnings, knowledge and skill sets are maximised across the teams and in collaboration with the five projects selected for funding under the Commissions fast-track exceptional procedure. To facilitate information sharing and collaboration, a Central Information Repository will be established under Topic 1. All projects under the Ebola+ programme are expected to contribute to that repository. Likewise, a Scientific Advisory Board as well as an Ethics Board will advise all projects under the programme and will be established under Topic 1.

The establishment of this Ethics Board under Topic 1 notwithstanding, all projects to be funded remain fully responsible for respecting all ethical requirements.

Projects to be funded must comply with all relevant European laws, regulations and rules as well as the laws of the countries in which the studies take place. Particular attention needs to be paid so as to ensure compliance with all ethical rules, notably those related to the conduct of clinical

investigations and clinical trials. Consortia are expected to interact with the EMA for advice on the conduct of trials and manufacturing–related questions[5] and when relevant with African regulatory bodies.

A template[6] is available to help applicants provide all the relevant information for the planned clinical studies. Use of this template is not mandatory and the necessary information for experts to evaluate the projects involving clinical trials can also be provided in the regular proposal template.

JUSTIFICATION FOR NON-EU IN-KIND CONTRIBUTION

In order to meet the objectives of the different topics under the Ebola+ programme, part of the in-kind contribution from EFPIA companies will originate from third countries other than countries associated to H2020:

- A range of expertise and resources of the participating EFPIA companies and of many companies' virology franchises that are necessary to carry out the key activities are placed in third countries other than countries associated to H2020.
- Clinical trials against Ebola and other filoviral haemorrhagic fevers will have to be conducted in endemic countries (typically in West Africa).
- Since activities are meant to progress development and access to products globally, regulatory expertise covering all geographies will be required.

CALL PROCESS

The current Call for proposals includes the first 5 topics under the Ebola+ programme. It is expected that additional Calls will be launched at a later time so as to address additional topics under this programme.

The current Call for proposals will follow a single-stage fast track process. Industry companies that are constituent entities of EFPIA or their affiliated entities and/or IMI2 JU Associated Partners contribute with in-kind and direct financial contributions. Academia, SMEs, hospitals, healthcare professionals, regulators, public health authorities, etc. are eligible to receive IMI2 JU financial contributions. Legal entities from across the world can participate and participants from the majority of potentially participating countries are eligible to receive IMI2 JU financial contribution[7], in

5 http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000624.jsp&mid=WC0b01ac0580841e30

6 http://ec.europa.eu/research/participants/portal/doc/call/h2020/h2020-phc-2015-two-stage/1620124-essential_information_for_clinical_studies_2015callsv2_18082014_en.pdf

7 list of countries described in Annex A of the general annexes to the general H2020 work programme 2014-2015: http://ec.europa.eu/research/participants/data/ref/h2020/wp/2014_2015/annexes/h2020-wp1415-annex-a-countries-rules_en.pdf

accordance with the applicable rules[8]. Applicant consortia need to fulfil the criteria as outlined in the Rules for participation applicable to IMI2 JU actions. To facilitate setting up consortia, the IMI2 JU provides a partner search tool[9].

All proposals evaluated under the 5 different topics will be ranked in one single list. Best-ranked proposals, in the framework of the available budget, will be invited to prepare a Grant Agreement.

INDICATIVE BUDGET

The indicative IMI2 JU financial contribution for the five topics mentioned in this call is up to EUR 140 million. EFPIA companies are expected to provide an in-kind contribution of around EUR 140 million.

8 http://www.imi.europa.eu/sites/default/files/uploads/documents/IMI2_Call1/Summary_of_provisions_for_particip_2014.06.26.pdf

9 http://www.imi.europa.eu/content/partner-search

TOPIC 1. VACCINE DEVELOPMENT PHASE I, II, III

TOPIC DETAILS

Topic code	IMI2-2014-02-01
Project type	Research and innovation action (RIA)
Submission & evaluation process	Single stage fast track

SPECIFIC CHALLENGE

In view of the current epidemic, the WHO has identified the progression of vaccine candidates currently in development as an urgent public health need. Several candidate vaccines are available. Prime/boost vaccine approaches are promising, as they may provide protection against Ebola infection that is of longer duration.

SCOPE

Design and implementation of Phase I, II, or III clinical development of vaccine candidates, including prime boost combinations against Ebola virus disease (Zaire), to start in early 2015. The applicants must have vaccine candidates available and demonstrate the ability to roll out clinical trial vaccination programmes in EU / Africa, and to conduct studies in areas where Ebola virus disease is endemic. The clinical development programme(s) need(s) to be aligned with the global effort coordinated by the WHO.

Proposals addressing Topic 1 must include plans to set up a Central Information Repository for the Ebola+ programme for sharing results, learnings and data both amongst Ebola+ partners and with the outside community. The information repository should include (but not exclusively be restricted to): The capability to capture basic experimental data via an electronic lab notebook; A pharmacological screening platform for the capture, analysis and sharing of assay data and a system for capturing, analysing and sharing translational/clinical data. Applicants should in the first instance re-use capabilities that have been developed in other IMI projects and new capabilities should only be developed where no other alternative already exists. Finally any solution should include a strategy that ensures the long term sustainability of the data so that it remains accessible to the scientific community beyond the time-line of the project.

In addition, proposals addressing Topic 1 should include plans to set up a Scientific Advisory Board including proposed membership representing key stakeholders to give scientific and strategic advice to both specific projects and to the overall programme. Likewise, proposals should include plans to set up an Ethics Board whose role would be to ensure that all activities carried out under the programme fully account for any ethical considerations[10].

10 Ethics pre-screening and ethics review - IMI2 Manual For Submission, Evaluation And Grant Award

It is considered that an IMI2 JU financial contribution of 70-110 million and an EFPIA in-kind contribution of EUR 10-20 million would allow this specific challenge to be addressed appropriately. Nevertheless, this does not preclude submission and selection of proposals requesting other amounts.

Clinical study designs and therefore costs are likely to be influenced by several external factors such as; evolution of the current outbreak in West Africa and the precise requirements of regulatory authorities.

EXPECTED IMPACT

The vaccine development programme(s) are/is expected to provide the data to assess the safety, immunogenicity and efficacy of the candidate vaccine(s) in preventing EVD. The projects are thus expected to have a major impact on global health, both at the individual and the public health level. Learnings from this programme will also have an impact on the worldwide capacity to quickly develop vaccines in situations of global public health emergencies.

SPECIAL INFORMATION

Since the implementation of Phase I, II, and III clinical trials is linked to manufacturing capability, projects funded under Topics 1 and 2 of this Call are expected to work in collaboration to ensure maximal impact.

TOPIC 2. MANUFACTURING CAPABILITY

TOPIC DETAILS

Topic code	IMI2-2014-02-02
Project type	Research and innovation action (RIA)
Submission & evaluation process	Single stage fast track

SPECIFIC CHALLENGE

In view of the current epidemic, the WHO has identified the progression of vaccine candidates currently in development as an urgent public health need. Because Ebola vaccines are recombinant adenovirus or other viral-based vaccines and need to be produced in facilities meeting an appropriate biosafety level, manufacturing the quantity of vaccine doses necessary for large-scale clinical testing and that can be thereafter urgently deployed represents a major challenge.

SCOPE

The project(s) will work on scaling up the currently available production techniques to the necessary scale and will be fully compliant with good manufacturing practices (GMP) and biological safety level requirements.

a. Costs and milestones are requested for manufacturing activities at volumes in the range of:
   - 100,000 – 250,000 vaccine courses
   - 250,000 – 2M vaccine courses
   - 2M – 20M vaccine courses

   Consideration to Drug Substance manufacture (formulated vaccine bulk) and finished Drug Product (vialed vaccine doses) should be given. Alternative manufacturing platforms to those currently utilised, or process improvement activities to increase vaccine manufacturing yields, may also be proposed.
b. Production and release of finished Drug Product is currently foreseen as a key bottleneck. Based on current regulatory requirements, non-replicating viral vaccine vectors need to be filled in BSL-2 compliant manufacturing facilities. This limits the number of manufacturers (CMOs and pharmaceutical companies) that are able to offer their services for fill and finish of an Ebola vaccine. Proposals are sought to generate additional data to help provide the necessary scientific, technical and regulatory justifications to seek a reclassification of such vectors such that they require BSL-1 containment, thereby opening up the potential for more manufacturers to assist in responding to the current outbreak.

It is considered that an IMI2 JU financial contribution of 10-20 million and an EFPIA in-kind contribution of EUR 70-110 million would allow this specific challenge to be addressed

appropriately. Nevertheless, this does not preclude submission and selection of proposals requesting other amounts.

EXPECTED IMPACT

The project will deliver a manufacturing platform to provide the capacity for producing the required number of vaccine doses in GMP quality. Getting this type of production capacity online will have impact more generally for European competitiveness in the area of biological production under appropriate biological safety level conditions.

SPECIAL INFORMATION

Since the implementation of Phase I, II, and III clinical trials is linked to manufacturing capability, projects funded under Topics 1 and 2 of this Call are expected to work in collaboration to ensure maximal impact.

TOPIC 3. STABILITY OF VACCINES DURING TRANSPORT AND STORAGE

TOPIC DETAILS

Topic code	IMI2-2014-02-03
Project type	Research and innovation action (RIA)
Submission & evaluation process	Single stage fast track

SPECIFIC CHALLENGE

Currently available vaccine candidates need to be stored and transported at low temperature to maintain activity. Maintaining these conditions for deploying the vaccine in the areas targeted for vaccination can be challenging.

SCOPE

The project(s) will develop tools and technologies to be able to distribute current Ebola vaccine candidates utilising existing vaccine deployment infrastructure while taking into account current stability features (e.g. the need for low temperature) and also taking into account real-world field conditions and the health systems context.

Proposals that cover stability testing and supporting analytical capabilities to be applied at all stages of the shipping, storage and deployment process are encouraged.

It is considered that an IMI2 JU financial contribution of approximately 2 million and an EFPIA in-kind contribution of approximately EUR 2 million would allow this specific challenge to be addressed appropriately. Nevertheless, this does not preclude submission and selection of proposals requesting other amounts.

EXPECTED IMPACT

Better availability of Ebola vaccines. Novel tools and technologies for distributing current vaccines that require very low temperatures for stability.

TOPIC 4. DEPLOYMENT AND COMPLIANCE OF VACCINATION REGIMENS

TOPIC DETAILS

Topic code	IMI2-2014-02-04
Project type	Research and innovation action (RIA)
Submission & evaluation process	Single stage fast track

SPECIFIC CHALLENGE

To control the epidemic, ensuring vaccination coverage is of critical importance. In addition, to ensure lasting protection, a booster dose with a heterologous vaccine may potentially be required. This creates additional challenges for compliance i.e. guaranteeing that the right vaccine dose is given at the right time. Furthermore, the countries mostly affected by the current epidemic experience a climate of distrust in vaccines. Lack of community acceptance represents a significant challenge that could potentially derail both vaccine trials and vaccine distribution.

SCOPE

The project will develop i) technologies and tools that augment the adherence to the vaccination regimen at individual level. It will also ii) look into environmental factors that impact compliance and look at how to favourably influence these at community level.

The project will be rolled out and operationalised during conduct of the large scale phase II and III vaccination trials conducted under Topic 1 of this Call to assess the safety and efficacy of a candidate vaccine. Those trials offer an opportunity to test and validate any new tools and technologies. One option can be to exploit the high penetration of mobile telecommunication and use of mobile apps in West Africa. Proposals that will use mobile communication strategies to increase awareness, acceptance and subject recruitment in the vaccination campaigns or will create specific apps to remind participants of their appointments and keep track of their response or side effects are encouraged. In this type of project it is essential to guarantee privacy of subjects. To that end the operation as such of the telecommunication infrastructure within the study needs to be clearly separated from the scientific work, for example by having different legal entities responsible for the different aspects.

Ethical considerations must also figure in the assessment, taking into account the health-systems context.

The project will develop specific tailor made communication programmes that should help with the overall acceptance of the vaccination programme, and increase the willingness of the community to fully comply with the vaccination regimen.

The scope of the project includes research on community vaccine acceptance and attitude towards vaccines.

Welcome are also considerations on how monitoring of adverse events could be put in place, and how vaccinees who get a fever should be handled.

It is considered that an IMI2 JU financial contribution of approximately 25 million and an EFPIA in-kind contribution of approximately EUR 25 million would allow this specific challenge to be addressed appropriately. Nevertheless, this does not preclude submission and selection of proposals requesting other amounts.

EXPECTED IMPACT

The proposed project is expected to provide a fully validated tool or system that captures critical information for each vaccinee (date, dose, batch no.), allows for automated recalls to the vaccinee for subsequent doses, central tracking of overall vaccination coverage and compliance, all in a user friendly, cost economic way.

Improved overall acceptance and a positive attitude towards vaccination programmes will facilitate the conduct of clinical trials in endemic regions, and will increase compliance and help to combat both the current epidemic and prevent outbreaks in the future.

TOPIC 5. RAPID DIAGNOSTIC TESTS

TOPIC DETAILS

Topic code	IMI2-2014-02-05
Project type	Research and innovation action (RIA)
Submission & evaluation process	Single stage fast track

SPECIFIC CHALLENGE

Rapid detection of Ebola infections in the field or at decentralised healthcare centers is an urgent need in the current crisis of the outbreak of EVD and will remain important even after the current crisis may have subsided. Additional technologies addressing various healthcare facilities settings will also be important to maintain surveillance in the long term. Current PCR-based tests have a number of limitations related to time and procedures requiring infrastructures and specific training. Tools and technologies are needed to provide quality diagnostics at low cost. Several such tests are already under development but their performance and practicability are unknown.

SCOPE

The project(s) will work on developing rapid diagnostics to detect EVD at acceptable costs and with very high sensitivity and specificity. At a minimum a rapid diagnostic test should be able to be deployed at decentralised health care facilities under conditions with minimum laboratory infrastructures available. Projects can work on validating existing tests or on expanding the use of tools currently being developed, through clinical validation to registration and launch. Projects must in any case include a phase of clinical validation in the field under real-world conditions, address manufacturing and access path to ensure sustainable distribution including taking into account ethical considerations and the health systems context. Any suitable technology can be used but the focus should be on practical solutions that meet the following criteria:

- Very high sensitivity and specificity
- Ability to be deployed in resource-limited settings
- Minimal training required to operate
- Capability of multiplexing in order to include different ebola strains
- Time to result 15-30 minutes (desirable) – 3 hours (acceptable)
- Sample type for intake: blood (capillary fingerstick desirable), other less invasive sample types (urine, etc.)

Additional capabilities to provide epidemiological monitoring (eg. Internet connectivity) would be valuable.

It is considered that an IMI2 JU financial contribution of approximately 7.5 million and an EFPIA in-kind contribution of approximately EUR 7.5 million would allow this specific challenge to be addressed appropriately. Nevertheless, this does not preclude submission and selection of proposals requesting other amounts.

EXPECTED IMPACT

Increased availability of rapid diagnostic tests for EVD, providing in a first step immediate impact on public health in regions where the disease is endemic.

Possible impact on business opportunities for European SMEs active in this area.

POTENTIAL FUTURE TOPICS UNDER THE IMI EBOLA AND OTHER FILOVIRAL HAEMORRHAGIC FEVERS PROGRAMME

IMMUNOTHERAPY

Ebola is a highly fatal disease, for which no efficient therapy is available today. There is increasing evidence that transfusion of blood from patients recovered from EVD has therapeutic effect, most likely related to the presence of neutralising antibodies, opening the potential for immune therapy. A potential future topic would be aimed at developing therapeutic products for filovirus infections based on passive immunisation (such as monoclonals, hyperimmune gammaglobulines, etc...), which should result in sufficient treatment regimens available at affordable price.

FORMULATIONS FOR COLD CHAIN

A potential future project will focus on the development of alternative formulations (for clinically active vaccines) that would improve thermo-stability to simplify the vaccine distribution logistics, taking into account real-world field conditions and the health systems context.

RAPID DIAGNOSTIC TESTS – LONG TERM

A potential future project would follow the initial effort (current Topic 5) of developing affordable rapid diagnostics to detect Ebola and other haemorrhagic fevers allowing long term surveillance. The project may address developing new tests through early development, analytical validation, clinical validation, registration and launch.

ANTIVIRALS DEVELOPMENT AND REPURPOSING

Ebola virus is a negative sense ssRNA virus with a 19kb genome encoding just 7 genes. As such there is comparatively limited scope for the development of anti-viral small molecules, with the polymerase and viral entry processes likely to form the most amenable druggable targets. There are also currently a very limited number of facilitates globally with the infrastructure to run CAT4 Ebola virus cell based assays, which is a critical component for progression of any repurposing program. A potential future topic would aim at creating a co-ordinated and collated tool-box of molecules from across the Industry, which are known to have anti-viral efficacy against a range of viral targets and may have been discontinued from development against their primary target. The project would seek to repurpose these molecules by testing in a CAT4 efficacy cell based Ebola virus assay, to determine whether these molecules have any utility in the blockade of Ebola viral entry or replication. If molecule(s) with potential anti-viral activity are identified, then depending upon their readiness for clinical development, a series of pre-clinical and clinical safety studies may be required to underwrite further clinical development.

MULTIVALENT FILOVIRUS VACCINE DEVELOPMENT

Multivalent filovirus vaccine candidates might be better able to protect against a range of current (Zaire) and future filovirus outbreaks. A potential future topic would aim at developing promising multivalent filovirus vaccine candidates. The project would deliver efficacy data in relevant animal models, toxicology data to support entry into clinical studies, and Phase I, II, and III clinical studies.

ACRONYMS

The following list of acronyms is applicable in the current call for proposals document:

IMI2 JU:	Innovative Medicines Initiative 2 Joint Undertaking
EVD:	Ebola Virus Disease
EFPIA	European Federation of Pharmaceutical Industries and Associations
WHO:	World Health Organisation
SAB:	Scientific Advisory Board
EAB:	Ethics Advisory Board
EMA:	European Medicines Agency
PCR:	Polymerase Chain Reaction
GMP:	Good Manufacturing Practice
BSL-2 Laboratory:	Biosafety Level 2 Laboratory
CDISC:	Clinical Data Interchange Standards Consortium
CMO	Contract Manufacturing Organisation
CAT-4:	Category 4
ssRNA	single-stranded RNA

CONDITIONS FOR THIS CALL

Applicants intending to submit a proposal in response to the IMI2 2nd Call should read the topic text, above, the H2020 Rules for Participation[11], the Commission Delegated Regulation[12], the IMI2 Manual for submission, evaluation and grant award[13] and the IMI2 RIA Evaluation Criteria[14].

Call Identifier: H2020-JTI-IMI2-2014-02-single-stage

Publication Date: 6 November 2014

Submission start date: 22 November 2014

Submission deadline: 1 December 2014 – 17:00:00 Brussels time

Indicative Budget: From EFPIA companies: around EUR 140 000 000
From the IMI2 JU: up to EUR 140 000 000

CALL TOPICS

IMI2-2014-02-01	The indicative contribution from EFPIA companies is EUR 10 to 20 million. The financial contribution from IMI2 JU is a maximum of EUR 110 million.	Research and Innovation action. Single stage submission and evaluation process. All proposals evaluated under the five topics will be ranked in one single list. Several proposals may be invited to conclude a grant agreement, depending on budget availability and their ranking.
IMI2-2014-02-02	The indicative contribution from EFPIA companies is EUR 70 to 110 million. The financial contribution from IMI2 JU is a maximum of EUR 20 million.	Research and Innovation action. Single stage submission and evaluation process. All proposals evaluated under the five topics will be ranked in one single list. Several

11 http://ec.europa.eu/research/participants/data/ref/h2020/legal_basis/rules_participation/h2020-rules-participation_en.pdf

12 http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ:JOL_2014_174_R_0003

13 http://www.imi.europa.eu/sites/default/files/uploads/documents/IMI2_Call1/Manual_for_submission_evaluation_grant%20award_2014.06.26.pdf

14 http://www.imi.europa.eu/sites/default/files/uploads/documents/IMI2_Call1/IMI2_C1_S0_Evaluation_form.pdf

		proposals may be invited to conclude a grant agreement, depending on budget availability and their ranking.
IMI2-2014-02-03	The indicative contribution from EFPIA companies is EUR 2 million. The financial contribution from IMI2 JU is a maximum of EUR 2 million.	Research and Innovation action. Single stage submission and evaluation process. All proposals evaluated under the five topics will be ranked in one single list. Several proposals may be invited to conclude a grant agreement, depending on budget availability and their ranking.
IMI2-2014-02-04	The indicative contribution from EFPIA companies is EUR 25 million. The financial contribution from IMI2 JU is a maximum of EUR 25 million.	Research and Innovation action. Single stage submission and evaluation process. All proposals evaluated under the five topics will be ranked in one single list. Several proposals may be invited to conclude a grant agreement, depending on budget availability and their ranking.
IMI2-2014-02-05	The indicative contribution from EFPIA companies is EUR 7.5 million. The financial contribution from IMI2 JU is a maximum of EUR 7.5 million.	Research and Innovation action. Single stage submission and evaluation process. All proposals evaluated under the five topics will be ranked in one single list. Several proposals may be invited to conclude a grant agreement, depending on budget availability and their ranking.

ELIGIBILITY AND ADMISSIBILITY CONDITIONS

The conditions are described in parts A, B and C of the General Annexes to the H2020 general work programme 2014-2015.[15]

EVALUATION CRITERIA, SCORING AND THRESHOLD

The criteria, scoring and threshold are described in the IMI2 Evaluation Criteria, with the following exception:

IMI2-2014-02-01 IMI2-2014-02-02 IMI2-2014-02-03 IMI2-2014-02-04 IMI2-2014-02-05	If a proposal fails to achieve the threshold for a criterion, the evaluation of the proposal will be stopped.

EVALUATION PROCEDURE

The full evaluation procedure is described in the IMI2 Manual for submission, evaluation and grant award.

The procedure for setting priority order for proposals with the same score is given in the IMI2 evaluation criteria.

CALL PROCESS

The current Call for proposals includes the first 5 topics under the IMI2 Ebola+ programme. It is expected that future Calls will be launched so as to address additional topics under this programme.

The current Call for proposals will follow a single-stage fast track process. Industry companies that are constituent entities of EFPIA or their affiliated entities and/or IMI2 JU Associated Partners contribute with in-kind and direct financial contributions. Academia, SMEs, hospitals, healthcare professionals, regulators, public health authorities, etc. are eligible to receive IMI2 JU financial contributions. Legal entities from across the world can participate and participants from the majority of countries are eligible to receive IMI2 JU financial contribution[16], in accordance with the

15 http://ec.europa.eu/research/participants/data/ref/h2020/wp/2014_2015/annexes/h2020-wp1415-annex-ga_en.pdf

16 List of countries described in Annex A of the general annexes to the general H2020 work programme 2014-2015: http://ec.europa.eu/research/participants/data/ref/h2020/wp/2014_2015/annexes/h2020-wp1415-annex-a-countries-rules_en.pdf

applicable rules[17]. Applicant consortia need to fulfil the criteria as outlined in the Rules for participation applicable to IMI2 JU actions. To facilitate setting up consortia, IMI2 JU provides a partner search tool[18].

All proposals evaluated under the 5 different topics will be ranked in one single list. Best-ranked proposals, within the framework of the available budget, will be invited to prepare a Grant Agreement.

The IMI2 JU would like to draw the applicants' attention to the fact that due to the fast-track nature of the current Call, the time available for the Grant preparation will be very short. Consequently, all organisations participating in a proposal invited to prepare a Grant Agreement shall be ready to provide in a timely manner the necessary supporting documents for their validation in the Commission system[19] and to nominate a Legal Entity Authorised Representative (LEAR). Please note that a Grant Agreement cannot be signed until all participants' information has been validated by the competent Commission service.

INDICATIVE TIMETABLE FOR EVALUATION AND GRANT AGREEMENT

	Information on the outcome of the evaluation	Indicative date for the signing of grant agreements
IMI2-2014-02-01 IMI2-2014-02-02 IMI2-2014-02-03 IMI2-2014-02-04 IMI2-2014-02-05	Maximum 2 months from the date of submission.	Maximum 1 month from the date of informing the applicants following the evaluation.

CONSORTIUM AGREEMENTS

In line with the Rules for Participation and Dissemination applicable to IMI2 actions[20] and the IMI2 model grant agreement, participants in Research and Innovation actions are required to conclude a consortium agreement within 6 months of the start date of each action.

17 http://www.imi.europa.eu/sites/default/files/uploads/documents/IMI2_Call1/Summary_of_provisions_for_particip_2014.06.26.pdf

18 http://www.imi.europa.eu/content/partner-search

19 http://ec.europa.eu/research/participants/docs/h2020-funding-guide/grants/applying-for-funding/register-an-organisation/validation-of-organisation_en.htm

20 Regulation (EU) No 1290/2013 of 11 December 2013 and Commission Delegated Regulation (EU) No 622/2014 of 14 February 2014.

SUBMISSION TOOL

Please note: The IMI electronic submission tool **SOFIA** (Submission OF Information Application) is to be used for submitting a proposal in response to a topic of the IMI2 2nd Call; no other means of submission will be accepted. SOFIA will be opened for submission of proposals on **22 November 2014**. Updates of the proposals may be submitted online until the Call submission deadline. Only the most recent version shall be considered for the evaluation procedure (including eligibility check).

To access the IMI electronic submission tool SOFIA, applicant consortia wishing to submit a proposal will need to complete a request for access to the tool.

Organisations willing to participate in a project proposal need to be registered with the Commission service and have obtained a 9-digit Participant Identification Code (PIC) at:

http://ec.europa.eu/research/participants/portal/desktop/en/organisations/register.html

For any successful proposal, all participants' information provided at the time of the registration needs to be validated by the Commission service. Please note that a grant agreement cannot be signed until all participants have been validated.