

The Innovative Medicines Initiative Ebola+ programme

The Innovative Medicines Initiative (IMI) Ebola+ programme was launched in response to the Ebola outbreak that struck western Africa in 2014-16. The comprehensive programme contributes to efforts to tackle a wide range of challenges in Ebola research, including vaccines development, clinical trials, storage and transport, as well as diagnostics and treatments. It is hoped that the programme will help to make a difference in future outbreaks. In addition to Ebola, the programme also addresses related diseases, such as Marburg. The programme currently has 10 projects with a total budget of over € 250 million.

About Ebola and related diseases

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. The virus spreads through direct contact with the bodily fluids of infected patients who are showing symptoms. It has an incubation period of 2-21 days, and it usually begins with flu-like symptoms, but rapidly progresses to multiple organ failure and internal and external haemorrhages (bleeding). It is fatal in between 25% and 90% of cases.

There is currently no licensed treatment against EVD, and the development of treatments and preventive measures such as vaccines is hampered by challenges including manufacturing-related hurdles, the stability of vaccines during transport and storage, vaccine deployment, and the time taken to diagnose cases of EVD.



Signpost to the Ebola vaccine trial clinic in Kambia, Sierra Leone

Credit: Anneleen Vuchelen, Janssen

Ebola is a member of the filovirus family of viruses, which also includes Marburg virus. Like Ebola, Marburg causes severe, often fatal haemorrhagic fever in humans and other primates (monkeys, gorillas and chimpanzees), and like Ebola, it is transmitted directly from one person to another. There is no specific treatment or vaccine against Marburg haemorrhagic fever.

The IMI Ebola+ programme

The 2014-16 Ebola outbreak in western Africa was unprecedented in its scale and geographical distribution. In total, around 29 000 people were infected during the outbreak, the vast majority of them in the west African nations of Guinea, Liberia, and Sierra Leone. Over 11 000 people died in the outbreak, including many medical workers.

The IMI Ebola+ programme was launched in November 2014, when the outbreak was at its height. Thanks to a fast-track procedure, the first eight projects were underway by the beginning of 2015, addressing key challenges in vaccine development and manufacture as well as the need for devices capable of providing a rapid yet accurate diagnosis. In December 2015, IMI launched a second, open Call on Ebola and related diseases. This has so far resulted in the launch of two additional projects, both of which focus on vaccine development.

Find out more about the programme: bit.ly/EbolaIMI

Testing new Ebola vaccines

There is an urgent need for licensed vaccines for Ebola. There are a number of vaccine candidates in development, and some projects in the IMI Ebola+ programme are generating the data needed to assess the safety and immunogenicity of different vaccine candidates and the level and duration of protection they actually offer against the disease.

The **EBOVAC 1 and 2** projects are assessing, through clinical trials in Europe and Africa, the safety, tolerability and immunogenicity (ability to induce an immune response) of the 'prime-boost' Ebola vaccine regimen (Ad26.ZEBOV and MVA-BN-Filo). In a prime-boost vaccine regimen, trial participants are first given a dose to prime the immune system, and then a 'boost' dose of another vaccine which is intended to enhance the immune response over time.

To date, the projects have vaccinated over 2 300 people in trials involving 21 centres across 8 countries (Burkina Faso, Côte d'Ivoire, France, Kenya, Sierra Leone, Tanzania, Uganda, UK).

Analyses from one Phase 1 study in the UK reveal that the immune response triggered by the vaccine lasts for at least one year; the findings were published in the prestigious *JAMA: The Journal of the American Medical Association*.

VSV-EBOVAC and **VSV-EBOPLUS** build on existing work to advance the development of the Ebola vaccine candidate VSV-ZEBOV ('vesicular stomatitis virus-vectored Zaire Ebola vaccine'). The projects are using cutting-edge technologies to carry out in-depth analyses of samples taken from clinical trial participants (including children) before and after vaccination. This allows them to gather vital information on both vaccine safety as well as the strength of the immune responses triggered by the vaccine.

Among other things, the scientists set out to find out which immune cells get activated early on, which inflammatory markers are released after that, and how this early activity later impacts the production of antibodies against the Ebola virus. In the process, they discovered a unique signature of the VSV-ZEBOV vaccine. The information could not only help predict adverse reactions and the effectiveness of this vaccine, but also inform the development of vaccines for other diseases as well.

One of IMI's newest Ebola+ projects, **PEVIA** aims to develop a novel Ebola vaccine that is easy to produce at scale, is cost effective, and can be easily transported and stored in affected areas.



Vial of Ebola vaccine
Credit: Alexandra Donaldson, LSHTM

Manufacturing Ebola vaccines

The focus of the **EBOMAN** project is on accelerating the development and manufacturing of the 'prime-boost' Ebola vaccine regimen.

The EBOMAN project created a new vaccine filling line that can generate batches of 30 000 vaccine vials faster than before. EBOMAN expanded Europe's manufacturing capacity for live bacteria and viruses, particularly for new experimental vaccines, with a biosafety rating of 2.

In the short term, the project provided the vaccines needed for the trials run through the EBOVAC1 and 2 projects. In the long term, Janssen Vaccines & Prevention B.V., one of the Janssen Pharmaceutical Companies of Johnson & Johnson, which is behind the vaccine regimen in partnership with Bavarian Nordic, holds a stockpile of 2 million Ebola vaccines in readiness for a future outbreak.

The German SME Vibalogics coordinated the project. According to their managing director, participating in IMI triggered the expansion of their business, brought in more customers, helped them to establish new partnerships, and increased their visibility on a global level. The company is now prepared to deliver thousands of vaccine doses for their partners whenever it comes to unforeseen outbreaks of devastating infectious diseases, for which new clinical candidates have to be developed and tested at short notice.

Ensuring people get vaccinated

For a vaccine to have a real impact on an outbreak, high levels of vaccination coverage are essential. However, the stigma surrounding Ebola, coupled with a suspicion of vaccines in general, could deter many people from getting vaccinated. Strong communication and community engagement campaigns are therefore needed to address these challenges. The **EBODAC** project's goal was to develop a communication strategy and tools to promote the acceptance and uptake of the 'prime-boost' Ebola vaccine regimen as part of a clinical study being conducted in Kambia, a rural district of Sierra Leone.

In order to build trust in the community, the EBODAC team, in collaboration with the EBOVAC1 team, employed many creative strategies, including radio shows, drama performances, and community meetings. The project maintained close contacts with local communities, so that concerns and rumours could be addressed rapidly. They also set up participant advisory groups, where trial volunteers could give feedback to the people running the trial.



*Idrissa Kamara receives the first vaccination in the EBOVAC Salone trial
Credit: Alexandra Donaldson, LSHTM*

The team also deployed innovative technologies to achieve their goals. Trial participants underwent biometric registration using fingerprint and/or iris scans, and their identity was verified at subsequent study visits. Appointment reminders were sent in local languages via mobile phone to ensure people didn't miss a clinic visit, and the second vaccine dose.

Thanks to EBODAC's efforts, over 450 adults and children received both doses of the vaccine regimen in the Sierra Leone study. Moreover, much of what was learnt during EBODAC could also be applied for vaccination campaigns for other diseases in other parts of the world.

Diagnose Ebola fast and on the spot

There is an urgent need for fast, reliable tests to determine if someone is infected with Ebola or not – the faster a patient is diagnosed, the faster they can be treated and isolated. The ideal test should be easy to administer; protect users from contact with highly-infectious bodily fluids; and work at the point of care, avoiding the need to transport samples or suspected patients to a treatment centre.

MOFINA drew on an existing automated device, Alere q, to develop a new method for detecting all known strains of Ebola as well as Marburg. The device only requires a finger-prick sample to run the test, and the system's compact design and battery pack mean it works well in remote areas. It gives reliable results in just 75 minutes and is already commercially available.

EbolaMoDRAD has developed diagnostic tools which have been or are being validated in the field with human samples. Their system uses vacuum tubes to inactivate the Ebola virus during sample collection, making it possible to handle samples safely outside high containment laboratories. Many of the tools developed within the project will also be used in future research projects.

FILODIAG has developed an Ebola detection system that delivers results in just half an hour and is capable of detecting even low levels of the virus. The system, which is currently being finalised, is designed to work in resource-limited settings. The team will run tests in Africa at the end of this year.

Capacity building

IMI projects are helping to build capacity in the countries affected by the recent outbreak by training people and building facilities.

EBOVAC1 delivered 213 training courses across a number of trial sites, including in Africa. In addition, staff at the Kambia Government Hospital in Sierra Leone received training in emergency and paediatric care. The project also built a new vaccine storage facility at the hospital, installed a research laboratory, and turned a disused room into an emergency room.

The **EbolaMoDRAD** project has also run workshops on subjects such as mobile laboratory deployment in outbreaks and outbreak management teams.



*Vaccine storage facility at Kambia Government Hospital
Credit: Tom Mooney, LSHTM*

About the Innovative Medicines Initiative (IMI)

IMI is a partnership between the European Union and the European pharmaceutical industry, represented by EFPIA. IMI was launched in 2008 with the ambitious goal of improving the medicines development process and making it more efficient so that patients will have faster access to better and safer medicines. IMI projects address challenges in medicines development that can only be addressed by collaborations involving all relevant stakeholders. Today, IMI's 85 collaborative projects are delivering promising results in disease areas that are all too familiar to many Europeans, including dementia, infectious diseases, and diabetes. Globally, IMI is recognised as a pioneer of open innovation and a model for successful public-private partnerships in research. IMI has a budget of over €5 billion for the period 2008-2020. Half comes from the EU's research and innovation programmes. The other half comes from large companies and organisations, mostly EFPIA companies. These do not receive any EU funding, but contribute to the projects 'in kind', for example by investing their researchers' time or providing access to research facilities or resources.