HUMAN VACCINES & IMMUNOTHERAPEUTICS
2018, VOL. 14, NO. 1, 14–16
https://doi.org/10.1080/21645515.2017.1356649

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PROFILE

European & Developing Countries Clinical Trials Partnership (EDCTP)

Ole F. Olesen

European & Developing Countries Clinical Trials Partnership, The Hague, The Netherlands

How and when did your organization start, and where are you located?

EDCTP was established by the European Union in 2003. The first EDCTP program ran until 2015 and focused on HIV, tuberculosis (TB) and malaria. It supported numerous clinical trials that aimed to have a significant impact on the diagnosis, treatment and prevention of these diseases. In light of significant unmet medical needs, the scope of EDCTP was extended in 2014, now covering neglected infectious diseases, diarrheal diseases, lower respiratory tract infections, and emerging and re-emerging infections affecting sub-Saharan Africa (such as Ebola virus disease and yellow fever), in addition to HIV, TB, and malaria. EDCTP has 2 offices, with its headquarter in The Hague, The Netherlands, and an African office in Cape Town, South Africa.

What are the most critical problems in vaccine/immunotherapeutics development in your field of interest?

The main problem in developing vaccines or immunotherapies for poverty-related infectious diseases is that many of the low-hanging fruits have already been harvested and we are left with some really tough challenges. Many bacterial and viral pathogens with stable surfaces have already been successfully targeted for vaccine development, like yellow fever, tetanus, smallpox and measles just to mention a few. Even Ebola would fall into this category as a presumably effective vaccine was developed surprisingly quickly once sufficient resources had been mobilised. We are instead left with rapidly evolving pathogens like HIV, mycobacterial diseases like tuberculosis and Buruli ulcer, not to mention parasitic diseases like malaria and leishmaniasis. To protect effectively against many of these diseases we will need to develop vaccines that can elicit a well-orchestrated immune response with a correct balance between humoral and cellular components. Despite many years of intensive research, despite hundreds of millions of dollars from public and private sources, our knowledge of the detailed human immune response, biomarkers and correlates of protection for prominent illnesses like AIDS, tuberculosis and parasitic diseases is still surprisingly scarce. The currently available knowledge is simply insufficient for intelligent selection of antigens and adjuvants that can generate an optimal immune response for these diseases. We are therefore still overly dependent on human clinical trials to select promising vaccine candidates, creating an obvious bottleneck in terms of time and resources required for vaccine development.

What is the mission of your organization?

EDCTP is focused on some of the greatest areas of unmet medical need in sub-Saharan Africa – infectious diseases. Although non-communicable diseases have become a serious concern in sub-Saharan Africa as well, the infectious diseases are still a heavy burden in most countries and among many poor populations. Globally, lower respiratory tract infections are responsible for more than 3.0 million deaths every year, TB 1.4 million, diarrheal diseases 1.4 million, HIV 1.1 million, and malaria about 850 000. Most of these deaths occurred in low-income countries. Particularly in sub-Saharan Africa the burden of infectious disease is highest. In addition, more than a billion people are affected by morbidity caused by the neglected infectious diseases.

Therefore, our mission is to reduce the individual, social, and economic burden of poverty-related diseases in sub-Saharan Africa. We aim to do this by supporting collaborative clinical research to develop accessible, suitable and affordable medical interventions. Support for the development of African clinical research capacity is inextricably integrated in our funding approach.

How does your organization facilitate vaccine/immunotherapeutics development?

One of the main bottlenecks for vaccine development is the clinical testing of new candidates. This requires patients, adequate clinical infrastructures and sufficient funding, and EDCTP aims to help with all of this. EDCTP is a non-profit organization with the primary goal of supporting clinical trials for new or improved medicinal products for poverty-related infectious diseases. With an annual budget of approximately 125 million Euro, EDCTP provides funding to clinical trials through competitive calls for proposals. The clinical trials must be performed in sub-Saharan Africa, where the patients are, and the trials must normally be performed by consortia that comprise research teams from several different countries in sub-Saharan Africa and Europe. The different research teams should complement each other in skills, experience and expertise, and thereby collectively form a critical mass of knowledge and infrastructure with the ability to implement complex clinical trial protocols.

CONTACT Ole F. Olesen olesen@edctp.org Anna van Saksenlaan 51, 2593 HW The Hague, Netherlands.

How does your organization engage national and international resources committed to vaccine/immunotherapy research?

EDCTP was established as a public-public partnership between the governments of several European and sub-Saharan African countries. Currently, a total of 28 countries participate in EDCTP as full partners. These countries, of which 14 are from Europe and 14 are from sub-Saharan Africa, are the "owners" of EDCTP and decide the overall strategy and priorities of the organization, in consultation with an independent Scientific Advisory Committee. This structure means that EDCTP receives direct input from the 28 partner countries, and also provide a unique forum for European and African countries to come together and define common research objectives in the area of poverty-related infectious diseases.

EDCTP operates a unique pooled funding mechanism for supporting clinical trials. The EDCTP partner countries have collectively committed more than 683 million euro, either in cash or in kind, to support EDCTP's activities over a 10 year period. The European Union, the largest single funder of EDCTP, will match this contribution with a similar amount, while we also hope to raise additional contributions from pharmaceutical companies, charitable foundations, product development partnerships, and other like-minded organisations. We hope therefore to reach a total financial volume of roughly 2 billion euro that will be used to support clinical trials and strengthening of clinical trials capacity in sub-Saharan Africa.

What important partnerships does your organization have?

Our most important partnership is undoubtedly with our 28 partner countries in Europe and sub-Saharan Africa. EDCTP provides direct support to clinical trials of new and improved medicinal products in sub-Saharan Africa, but we also work closely with our partner countries to align and coordinate their national research investments in global health priorities. Every autumn we ask our partner countries to submit information about their intended public investments in global health research of relevance to EDCTP for the coming year. These Participating States' Initiated Activities (PSIAs), as we call them, are then compiled and analyzed by EDCTP to identify any potential synergies between the national activities of our partner countries. Where clear synergies are identified, either between the national activities of 2 or several countries, or with EDCTP's own activities, we then actively encourage closer collaboration and coordination between the parties involved. This approach has, as an example, resulted in the recent joint funding between EDCTP and the UK's Joint Global Health Trials partnership (JGHT) of 2 major clinical trials in sub-Saharan Africa for, respectively, the chemoprophylaxis of malaria during pregnancy and for the treatment of cryptococcal meningitis among HIV-infected individuals. The total investments in these 2 trials amount to more than 17 million euro, and the magnitude and potential impact of the trials have been greatly enhanced by the collaboration.

In addition to our partner countries, we also have active partnerships with several other organisations from both the private and public sector. This year we have planned to launch a joint call for proposals with the pharmaceutical company Glaxo SmithKline (GSK) to support talented African scientists to undertake clinical research in comorbidities between infectious and non-communicable diseases. Another partnership worth mentioning is our long-term partnership with the Special Programme for Research and Training in Tropical Diseases (TDR) and the European Federation of Pharmaceutical Industries and Associations (EFPIA), where we offer fellowships to African scientists that would like to improve their skills by working for a year in a pharmaceutical company in Europe.

What is your position in the organization?

I am director of North-North cooperation at the European headquarter of EDCTP. In this position I am deputising and assisting the executive director on activities related to European affairs and scientific matters. This involves responsibility for the operational aspects, including the implementation and oversight of our research investments in clinical trials, as well as contributing to the development of the EDCTP funding strategy. The other part of my responsibilities include the establishment, strengthening and maintenance of close collaboration with our strategic partner organizations in Europe and globally.

What "highlights" would you select in recent vaccine/immunotherapy research, development, or use?

I would highlight 2 recent events of major importance for vaccine and immunotherapy in the area of global health research. The first of these is the recent approval for human use of the first malaria vaccine for humans, namely the RTS,S vaccine. This vaccine is far from perfect. It has a limited protective effect, probably in the range of 30–50% and it probably has a rather limited duration and may only work in young children of 6 weeks to 17 months. Nevertheless, it represents a major scientific and conceptual breakthrough. RTS,S is the first vaccine that has ever been developed against a parasitic disease in humans, and it may therefore serve as a model and inspiration for improved vaccine candidates in the future, both for malaria and for other parasitic diseases.

The second highlight is the rapid development of an Ebola vaccine candidate. This is not because of the scientific breakthrough. It was somehow expected in the scientific community that an effective vaccine against Ebola virus disease could be developed on the basis of existing knowledge and technologies, but the speed of the development has been amazing. Developing a new vaccine will normally take an average of 10–15 years, but in the case of Ebola it has been done within a time span of 2–3 y. Admittedly, preclinical versions of both the rVSV-ZEBOV vaccine from Merck and the cAd3-EBO Z vaccine from GSK were available before the outbreak of Ebola virus disease in West Africa, but the most complicated, time-consuming and expensive part of vaccine development is normally the clinical trials, not at least when these have to be done in resource limited settings with inadequate infrastructures. It is therefore a huge achievement, and really a global achievement involving scientists, funders, companies, health care workers and - most importantly – patients and volunteers coming together from

across the world, that we could move from preclinical testing to an effective vaccine that is ready for regulatory submission within less than 3 y.

What areas or topics does your organization currently focus on?

Against the mission backdrop I sketched above, EDCTP aims to focus on closing research gaps to accelerate the development or implementation of medical interventions. These gaps are identified through consultation with other organisations active in relevant areas, experts on the various aspects and diseases of our scope, and our independent Scientific Advisory Committee. This information results in an annual research agenda clearly identifying priorities. These are taken into consideration when we plan the next calls for proposals for the annual work plans. To ensure a long-term perspective, we are implementing an overarching 3-y planning cycle. It is essential to support both long-term development of products or interventions and remain flexible to take advantage of new opportunities. Thus, the best place to look for what EDCTP focuses on, are the calls for proposals. For example, this year, we particularly aim to boost research on neglected infectious diseases, which is an area where little investment is made by other funders of the pharmaceutical industry, while our Scientific Advisory Committee has further recommended diagnostics, malaria drugs and vaccines, and tuberculosis vaccines as potential priority areas for the coming years.

What are your main goals for the next 5 years?

We set ourselves ambitious goals for a program that ends in 2024. We work to achieve a range of specific objectives by the end of it. Our main goals are to have funded by then at least one completely new medical intervention and to have contributed through the research we funded to at least 30 guidelines for improved or extended use of medical interventions. The clinical development of at least another 20 medical interventions should have progressed to the next phase of its clinical development. This would be the core achievement. Moreover, we will have made tangible contributions to stronger clinical research capacity in sub-Saharan Africa as well as its capacity to review and supervise clinical research among its populations.

All this is not possible without international collaborative research in Europe, in Africa and between European and African researchers. Therefore, the program will also have supported the alignment of national public investment in research on poverty-related infectious diseases. To that end, of course, we aim to involve more countries in Europe and sub-Saharan Africa as members of EDCTP.