



TBVI

TuBerculosis Vaccine Initiative

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TuBerculosis Vaccine Initiative (TBVI) facilitates the development of safer, more effective vaccines to protect future generations against tuberculosis.



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New vaccines: a reality for the next decade



Having moved into a pivotal new era, 2010 has been a remarkable year for the TB vaccine world. During the past decade, the portfolio of prospective new vaccines has expanded markedly. Worldwide, 12 vaccine candidates have entered clinical trials and several more are on their way. New TB vaccines could very well be realised within the next decade. Now we face the challenge of finding the capacity and the resources to execute the clinical trials needed and to make new vaccines available for those who need them most.

Over the past years, we have discovered that it has become increasingly difficult to mobilise the resources needed to bring vaccines from laboratories to the market. Therefore, in 2010, TBVI developed an innovative funding plan that will ensure new TB vaccines become a reality by 2020 (see page 7). I am glad that European politicians embraced the resolution to support this plan with an overwhelming majority, and I hope that in the coming year we will get the green light for this unique funding model.

The 'TB vaccine pipeline' looks more promising than ever, yet we must continue to innovate the first part of this pipeline: the discovery work in the laboratories. We must invest in new technologies to develop vaccines that also protect latently-infected people from getting tuberculosis, and vaccines that block infection and transmission. Furthermore, we should not forget about the search for biomarkers, which are necessary to monitor the effectiveness of new vaccines. While clinical trials are progressing, it is becoming more and more important to find the right assays to predict the protection rate of a vaccine candidate.

New vaccines are within sight, and that is good news. Nonetheless, much work still has to be done. I am very happy that this year, with the financial support of the European Commission, we have been able to start our NEWTBVAC project. In this project, which brings together 35 of our research partners, we will focus on the discovery of new vaccines, and prime-boost and other combination strategies. Furthermore, the discovery and development of new biomarkers is one of the pillars of this project.

"TBVI developed an innovative funding plan that will ensure new TB vaccines become a reality by 2020."

To ensure that only the most promising new vaccine candidates are supported, coordination is needed. TBVI, together with its USA-based partner Aeras, therefore started to define clear criteria which will be used to select vaccine candidates before they enter the next steps in clinical research. This fruitful collaboration between the world leaders in TB vaccine development will lead to very efficient use of investments by donors and the fastest possible progress in developing new, effective and safe vaccines for the world.

It is only thanks to the support of Wageningen University and Research Centre that TBVI could develop during its first years of existence. I am very proud that in 2010, TBVI was ready to continue as a fully independent foundation.

A new Governance Board was established with distinguished members and led by Onno Ruding, former Minister of Finance of the Netherlands. Finally, I would like to thank our donors and all others that in any way support our cause.

Jelle Thole, Director TBVI



Creating new ways to fund research



European researchers have made tremendous progress in the development of tuberculosis vaccines over the past ten years. Nevertheless, these projects risk being put on hold because of lack of resources. Unfortunately, the usual funding mechanisms are insufficient. TBVI has therefore developed a new funding model that will allow promising discoveries to be translated into actual vaccines.

“This model is quite unique and innovative,” says TBVI’s Vice President, Joris Vandeputte, one of the architects of the financial plan. “The plan shows a new way to invest in solutions for a poverty-related disease, tuberculosis. It changes the paradigm of market perception and the way of funding. We found that there is market potential, ensuring access to new tools by those who need them most. New tools can be developed at no cost for the taxpayer and with minimal risk for the state budget.” The financial model benefits many parties; it combines worldwide poverty reduction with the creation of a knowledge-based society, strengthening North/South, South/South and East/West collaborations. “It’s a practical and tangible fill-in of the European Union’s 2020 Agenda and Innovation Flagship Initiative,” adds Mr Vandeputte.

TBVI calculated a critical financing gap of €560 million, needed to bring the first, most advanced vaccines out of its portfolio to the market around 2020. In the plan, European governments or agencies are asked to provide guarantees to make it possible for TBVI to gradually withdraw money from financial institutions, in successive steps according to the progress of vaccine developments. Countries will thus not have to provide any cash; the investment will be spread over a minimum of ten years and the loan will be repaid through the sales of the marketed vaccines.

Through TBVI’s funding model, the chances of delivering a vaccine to the market are greatly improved. Obviously,

new vaccines would save the lives of millions of people, but the plan has more selling points. One of the strengths of the model is that it provides Europe with an opportunity to take a leading position in innovation. Mr Vandeputte explains: “European governments have committed to invest 3% of their Gross National Income in innovation. This commitment clashes with efforts to control and bring down state deficits. Our funding model offers a solution to governments and governmental agencies that are squeezed between budget restrictions and the commitment to support the knowledge-based economy and to increase health and wealth in the world.”

“New tools can be developed at no cost for the taxpayer and with minimal risk for the state budget.”

Joris Vandeputte, however, has more arguments that support the plan. Developing European vaccine candidates into concrete products has the advantage that previous investment and knowledge gained do not go to waste. And what is more: “Considering the threat of drug-resistant forms of tuberculosis, new vaccines will make us independent in having the tools to protect our citizens against the disease, as well as people all over the world.”



“Now is the time to sow if we want to reap in the future and leave a competitive economy to the next generations.”



Is it realistic to present any funding proposal, however innovative, in the current economic climate? Joris Vandeputte is convinced it is: “Precisely because of the economic climate. This plan is one of minimum risk; no cash is asked for from governments and it involves a very responsible way of handling money. Now is the time to sow if we want to reap in the future and leave a competitive economy to the next generations.” Members of the European Parliament received the financial plan with enthusiasm; in early 2011, the parliament accepted a resolution to fight tuberculosis, invest in new vaccines and support TBVI with an overwhelming majority.”

For European governments and governmental organisations to support this plan and commit to serious investment would mean a great breakthrough to tuberculosis vaccine research. “We step away from the idea that problems such as tuberculosis can only be solved through large grants,” explains Mr Vandeputte. “It is, to my knowledge, new to create a real business case for a poverty-related disease. It’s only now that the market opportunities have become clear.”

Political support for the plan has been growing and will continue to grow stronger in 2011, and Joris Vandeputte’s wish is that this will be followed by a quick roll-out of the plan. “Within TBVI’s portfolio, 11 vaccine candidates are already waiting for funding to be further developed. If funding is not found, they risk being lost, a situation that would be unthinkable for Europe and the world.”



Let us not run previous investments to waste



No, he was not aware of the reemergence of the problem of tuberculosis, but when Onno Ruding heard how serious the situation actually was, he did not hesitate and accepted the invitation to become chair of TBVI's Governance Board.

TBVI is proud to have him on board. Retired Vice-Chairman of Citibank and former Minister of Finance of the Netherlands, Mr Ruding has a wealth of experience when it comes to governance as well as finances. "Obviously, I have no specific knowledge of tuberculosis, but an organisation such as TBVI also needs people who know about governments, decision making and finance; someone who knows their way around in Europe, someone who can open doors."

Onno Ruding had never dealt with tuberculosis, but as it happens, he actually has quite a connection to the issue. "There are many doctors in my family, as well as in my family-in-law. My father-in-law was the director of a large TB sanatorium in the Netherlands and my own grandfather was the chairman of the board there. By the time my father-in-law retired, tuberculosis had almost disappeared from the Netherlands. It is an extra motivation for me that my family has such strong ties with the issue."

"Tuberculosis is not only a human disaster, it is also an enormous drain on the global economy," says Mr Ruding. He calculates that "The economic loss amounts to 0.52% of the world's Gross National Income. The cost of treatment for European citizens alone is already two billion euros per year. Developing new vaccines is the most cost effective way to eliminate tuberculosis. Moreover, it stimulates the knowledge-based economy."





The opportunity to wage war on a terrible disease is incredibly important to Mr Ruding. The way tuberculosis hampers development is another strong reason for him to support the search for new vaccines. However, Mr Ruding can present a list of additional factors that make it important for him to promote investment in new TB vaccines. "Innovation, European research and development, competition; we have a basis and we have a network. It would be such a waste not to finish the job. We have invested a lot already; if we don't continue, that investment will leave Europe. There's no doubt about that."

experience and reputation, I have to take things seriously. The problem is complicated and large. TBVI's financial plans amount to millions of euros. Isn't it not only a legal obligation but, more importantly, my moral duty to take that seriously? Imagine something went wrong and I said 'Well, I didn't have time to read.' Not a very strong excuse, is it?"

Onno Ruding hopes to support TBVI in three different areas: governance, financial management and political contacts. "I don't think there are many people with a combination of these elements. That comes with a certain age and the range of positions I have had. I don't have much to say about the medical, biological or pharmaceutical side of the story, but I will certainly try and put my network and knowledge to good use."

"2011 will be a kind of crossroads for TBVI," predicts Mr Ruding. The new funding plan, developed by TBVI, is a very important instrument with which to realise the development of two new vaccines by 2020. Mr Ruding explains: "If we can get guarantees for the resources needed now, we won't have to go begging over the next couple of years. That makes 2011 a crucial year."

Looking ahead, Onno Ruding concludes that "Creating new vaccines is a long-term process. We have to keep this going for another ten years or so. Hopefully, we will have reached our goal by then. If we stop investing before that, we will run all that previous investment to waste."

"The cost of treatment for European citizens alone is already two billion euros per year. Developing new vaccines is the most cost effective way to eliminate tuberculosis. Moreover, it stimulates the knowledge based economy."

A "true financial man", he calls himself. 'Thorough' seems to be a concept that fits him well too. In front of him is a stack of paper, riddled with lines and remarks; he is known for being well prepared. "I wouldn't do it otherwise," says Mr Ruding. "I made myself available to TBVI. With my



A golden future at an affordable price



Fantine, one of the lead characters of Victor Hugo's Les Miserables, died of tuberculosis, and German writer Franz Kafka also suffered from the disease. John Bowis, a member of TBVI's Council of Trustees, can present a whole list of people and characters who struggled with TB. He wants politicians and decision makers to understand that the disease is still a threat nowadays. "I believe that one should bring these things to life by talking about real people. Having worked in health, I have seen TB on the march. It's come back with a bang and it is worse because of drug resistance."

As a former Minister of Health and former MEP, John Bowis can see the reality of tuberculosis in his own backyard. "There is a threat of drug-resistant tuberculosis coming from Eastern Europe, but TB is also on the rise in London. It is a sad thing to be called the tuberculosis capital of Europe." Mr Bowis did not become a member of TBVI's Council of Trustees by coincidence; he has been involved in numerous campaigns aimed at combating tuberculosis and drug-resistant TB. "There are many health issues that I feel strongly about," says the former politician. "I'm mostly drawn to unresolved issues and to diseases with a stigma. TB is one of those and there is a great need for new vaccines."

"Politicians and decision makers need to understand that this is no past-tense disease," says Mr Bowis. "It's not geographically 'over there'. It's here and it's getting worse." Although that picture is a bit grim, John Bowis is not pessimistic about the future. "We are within striking distance of making a real difference by fighting a disease that affects many people. TB is colossal and it's frightening, but it need not be, because advances in medical science are opening doors." Those advances need attention and funding, and TB's voice might not always be loud enough. "There are always short-term threats that make it to the headlines, and diseases that threaten the better off. Still, what is very persuasive is that we have an offer; TBVI's new funding model holds up a golden future at a price that governments can afford and that will even allow them to save money."

"Politicians and decision makers need to understand that this is no past-tense disease. It's not 'over there'. It's here and it's getting worse."

Investing in new vaccines against tuberculosis is not only a cost-effective way to beat the disease; it is also good for Europe's position in the field of innovation. Mr Bowis: "Health in all its forms is an enormous contributor. Being the first in something is important. Europe has an opportunity to lead in terms of innovation. Health is not just a cost, it can be an investment; there is real potential for new vaccines. We're not asking for donations, we're not holding up the begging bowl. It's investment with return."

Will European politicians see the advantage of investing in new vaccines? Mr Bowis is certainly hopeful. "They need to understand the importance of health for economic policies; the real opportunities, the promise of a better future. I see a growing understanding. Competition might be a bit irritating sometimes, but it's also a good thing. We need to push each other a bit. It's all there, but now it needs to be drawn together."



Progress in research



Several promising vaccine candidates, vaccine-enhancing adjuvants and new biomarkers were the successful harvest of the TBVAC project that finished in December 2009. TBVI is now managing its successor NEWTBVAC, an exciting research network, funded by the European Union under Framework Programme 7. The project involves around 35 universities, research institutes and industries, mostly from Europe. Prof. Stefan Kaufmann, Chair of the Steering Committee of NEWTBVAC, explains its set-up and progress.

“The appeal of the NEWTBVAC project is that we cover a whole field, from research in the wet lab to translation into clinical trials,” says Prof. Kaufmann. “There are projects that focus on an actual product, like a vaccine, and there are research groups funded to do basic research or targeted research; we work from discovery to vaccine development.”

There is good reason to be positive. “I think that having 12 candidates in clinical trials worldwide is a breakthrough that nobody would have thought of 20 years ago,” says Prof. Kaufmann. “Most of these vaccine candidates come from Europe, and the vast majority received support through TBVAC and NEWTBVAC. We can surely say that we have made a quantum leap in TB vaccine research.” With so many candidates, it could be argued that it would be better to stop investing in discovery and to focus on developing a final vaccine. However, that is not NEWTBVAC’s standpoint, Prof. Kaufmann explains. “Our success is very much based on increased knowledge. Through the vaccines that are now being tested, we learn what they can and cannot do and how to improve new candidates.”

In 2010, existing challenges remained. Prof. Kaufmann: “We don’t know what vaccine will ultimately be protective in a satisfactory way. With some diseases, such as malaria, you can challenge people experimentally in vaccine trials. We cannot do that with tuberculosis and testing efficacy is more challenging and lengthy. Having biomarkers that would predict the efficacy of vaccines at an early stage would be a great solution.”

“I think that having 12 candidates in clinical trials worldwide is a breakthrough that nobody would have thought of 20 years ago.”



The NEWTBVAC project saw several highlights in 2010. “We now have some new adjuvants that had not been tested before,” says Prof. Kaufmann. “Furthermore, we are now focussing not only on pre-exposure, but also on post-exposure vaccines. We have data coming up, for example, from the H56 vaccine. This had not been looked at carefully enough before, so that is clearly an important step that we took in 2010.”

The H56 vaccine is a candidate developed at the Statens Serum Institut in Denmark. The vaccine attracted global media attention when its successful research data were published, and the vaccine is expected to enter clinical trials soon. MVA85A, developed by Oxford University and often described as ‘world leading’ remains the most clinically advanced vaccine candidate and has recently entered Phase IIb trials. Within NEWTBVAC, the valuable findings and experiences from this research are fed into researching new combinations of antigens and vectors. At the Max Planck Institute for Infection Biology in Germany, VPM1002, a genetically modified BCG vaccine candidate, made good progress. The candidate successfully passed a Phase I trial in Germany and is the most advanced live vaccine candidate for the replacement of BCG.



Dr Helen McShane:

“In 2010, there was a huge effort made by the South African Tuberculosis Vaccine Initiative (SATVI) to recruit for the Phase IIb infant trial with MVA85A. The target for enrolment was 2784 infants, a target which was achieved on 28th April 2011,” says Dr Helen McShane, who leads the TB vaccine programme at Oxford University.



Dr Germain Puzo:

“Usually in vaccinology the development of sub-unit candidates against intracellular pathogens is protein-based,” explains Dr Germain Puzo of the Institute of Pharmacology and Structural Biology (CNRS) in Toulouse. His research has a different approach; using lipid antigens, his team is trying out a new route to stimulate T-cells with the aim to develop sub-unit vaccines based on lipid antigens.

“Vaccine candidate MVA85A: a perfect example of how collaboration is needed.”

MVA85A is currently the most clinically advanced TB vaccine candidate and could become the first available vaccine, if the efficacy trials are successful. The vaccine candidate is a perfect example of how collaboration is needed; during its development the vaccine has been funded by a range of parties and clinical trials have been organised in collaboration with various African partners.

Dr McShane is excited about the efficacy trials: “It’s a big shift in focus. We don’t know whether the animal models predict efficacy in humans or not, and because we don’t have a defined correlate of protection, we can’t find out whether or not this vaccine works without testing it in efficacy trials. These trials represent a huge collaborative effort but will yield a lot of important data which will advance the field. The completion of enrolment of this infant efficacy trial is a major milestone for the field.”

Dr Puzo: “The envelope of *Mycobacterium tuberculosis* (*Mtb*) is composed of large amounts of lipids. Moreover, the structures of most of these lipids are unique in this bacterial genus. These lipids play a key role in the modulation of the host immune responses as ligands of the host pattern recognition receptors but also as antigens of human unconventional T-cell populations. So we are now trying to identify the lipids that stimulate the T-cell response.”

The characterization of the repertoire of the *Mtb* lipid antigens is the first step. The next step is how to deliver these lipid antigens to animal models for protection evaluations. Another challenge is how to combine these lipid antigens to enhance vaccine protection. “2010 was an important year. For the first time we demonstrated that the subunit vaccine Lip1 composed of *Mtb* glycolipids protects in guinea pigs against TB infection. However, this protection was not confirmed by a second campaign.” The team is hoping that they will be able to prove that lipids protect in animal models in 2011.



Biomarker research: complicated but crucial



Why do some people develop active tuberculosis while others don't? How do factors such as HIV, immunosuppressive therapies and antituberculosis treatments affect this? How much protection do new vaccine candidates offer, and in whom? An understanding of how disease works, who is protected and why, would be incredibly helpful in the search for new vaccines. Once potential new vaccines have been found, this understanding will also be important for determining the efficacy of the vaccine. For this reason, the search for biomarkers plays an important role within TBVI's research priorities.

For tuberculosis, there are currently no biomarkers available at all. The indicators would be helpful in predicting treatment success in patients with active TB, they could indicate whether people are at risk of a latent infection developing into an active infection, or they could predict levels of protection. With the increasing number of clinical trials, it is becoming more urgent to find biomarkers that can indicate protection.

The concept of biomarkers is rather abstract. Dr Hazel Dockrell, from the London School of Hygiene and Tropical Medicine, compares the immune system to a quiet pond with a calm, regular pattern: "Infection changes that pattern and we want to be able to monitor those changes. In this case, we're looking for something you can measure in a person that shows whether they are protected against developing the disease. The problem is that we don't know exactly what we're looking for."

Without biomarkers that can measure protection, researchers in clinical trials have to monitor very large groups of immunised volunteers for several years. Biomarkers could simplify this process and provide valuable information, not only with respect to efficacy but also to the ideal dosage, immunisation schedules and delivery tactics. Dr Dockrell: "We know, for example, that the BCG vaccine works well in some people in some places. What we don't know is when, where, how and why. I look for patterns of immunity in the blood, patterns that can distinguish people who are protected from those who are susceptible."

Research carried out in the past year has given Dr Dockrell a better idea of what to look for: "My take on 2011 is that we are now in the era of biosignatures. We know that measuring some individual candidate biomarkers such as IFNg is not good enough. Biosignatures, composed of a number of biomarkers, are likely to be more useful."

On a more technical level, Dr Dockrell explains: "These biomarkers can be measured within cells using intracellular cytokine staining and cell phenotyping, within serum/plasma or cell culture supernatants using multiplex bead array assays, or by analysing a number of genes simultaneously. For me, the biggest finding in 2010 was probably that measuring IFNg is not a predictive biomarker and that it is likely to be informative to measure innate as well as antigen-specific T-cell biomarkers. This was found by Anne O'Garra and her team at the National Institute for Medical Research in London."

TB vaccine research has made remarkable progress. Does that positively affect biomarker research? "We do have a unique opportunity now," says Dr Dockrell. "But there are immense challenges. Current trials are still in early phases so they don't involve enough people to get sufficient sampling. We need better ways of dealing with samples. A bag of money would certainly be helpful!"



Why supporters team up with TBVI



“Tuberculosis is a true global issue; we have to think increasingly on a global scale. That also means that every research product can potentially serve every human being.” Jorge Soares is Director of the Health and Human Development Department of the Gulbenkian Foundation, one of TBVI’s new donors, and he is passionate about supporting the fight against TB.

“We absolutely need a more effective vaccine against tuberculosis,” says Prof. Soares. “TB is developing more aggressive, drug-resistant strains of the bacterium. That’s why we support research. We are fighting disease in several developing countries and we can see the need for new vaccines.”

In 2010, TBVI welcomed the Calouste Gulbenkian Foundation as one of its new donors. The foundation supports vaccine research through TBVI. The foundation’s Director of Health is enthusiastic about TBVI as an organisation. “We concentrate on good ideas and good projects. We want to work with those who can potentially be innovative and who may have impact. We want to support active players. TBVI is innovative because it’s a cooperation network; we need more cooperation. TBVI has shown to be a reliable initiative and, what we like is that it started very much bottom up.”

“The support of European foundations is important to TBVI,” explains TBVI’s Resource Mobilisation Officer Danielle Roordink. “They play an important role in supporting innovative research initiatives on a national level but also increasingly across borders. TBVI has a strong pan-European network of scientists. Together with European foundations, TBVI will be able to strengthen the important research activities of this network.” Ms Roordink adds: “The foundations can help create awareness of the need for TB vaccines at national and European levels.”



Prof. Soares: “Gulbenkian was not aware of the problem of TB, but now we should be more and more committed to this type of problem. These issues require cooperation and networking, and we should create some advocacy.”

Many European foundations come together regularly through a platform called the European Foundation Centre. Could Gulbenkian’s involvement with TBVI open doors to other foundations? Jorge Soares can see a kind of overlapping in the areas that foundations focus on. “Foundations used to support the arts, poverty and social issues. Now we see more and more that they are starting to look at health at a global level. I think we can do some work to persuade other foundations to pay attention to the problem of TB.” Support doesn’t necessarily have to take place in the form of grants. Danielle Roordink of TBVI



explains: "For example, European foundations have been involved in the organisation of events, supporting us with a venue, paying for airline tickets and playing a role in communications and the opening up of their networks. The options are endless."

"How could society let it get to this point?" wonders Prof. Soares. "We have a vaccine that is almost a hundred years old and which has never been improved or replaced. The search for new vaccines against tuberculosis is important and I see a role for European foundations in supporting this fight. TBVI is a European network so we have responsibilities from our past."



2010 also brought tighter relationships with the pharmaceutical and biotech industry. TBVI is happy to receive the support of three sponsors from this industry: GSK Biologicals, Institut Mérieux and FIT Biotech Ltd. Why have these organisations teamed up with TBVI?

Geneviève Inchauspé, head of Transgene Infectious Diseases Research at Institut Mérieux: "TB is a real and everyday threat for fragile populations, but also more and more for European and developed countries' citizens, due to the spread of resistant strains. With Transgene, Institut Mérieux is supporting and encouraging the strong commitment of TBVI in its crusade to develop, in parallel, different approaches to therapeutic vaccines, seeking the more efficient ones in order to bring a definitive answer to this epidemic."

Gérald Voss, GSK Biologicals: "GSK is committed to the global fight against TB and is supporting TBVI in its mission to accelerate the development of vaccines against this disease. Why? Because we believe vaccines are a crucial part of this fight, which must result in the elimination of TB by 2050. Developing vaccines is not just an act of charity. It fills real market needs and there's no better way to match medical and human needs worldwide and stay at the edge of innovation."

Kalevi Reijonen, CEO and President of FIT Biotech Ltd: "FIT Biotech has developed innovative technology which significantly increases the efficacy of DNA vaccination. Our partnership with TBVI will make it possible to translate this technology into concrete new vaccines against tuberculosis. TBVI represents opportunities to get into a large network of experts which have developed a very promising vaccine portfolio."

Go to the root of the matter, with new vaccines



“Why do we need vaccines to control tuberculosis? We have to deal with cases where drugs do not or hardly work. And we have the problem of HIV/TB co-infection.” To Michel Greco, chair of the Stop TB Partnership Working Group on New TB Vaccines, the story is very clear: “Drugs are important, but we have to go to the root of the matter, with new vaccines.”

Michel Greco looks back at a rather successful year, for his working group as well as for TBVI. “In 2010, TBVI emerged as an important player on the TB vaccine market,” he compliments. Asked for his highlights, he speaks about collaboration, agreements and advocacy: “I’m not a scientist, I can’t tell you much about the progress in research but I was happy to see that several candidates progressed to new phases. My one and only task is to bring parties together and get them to talk and work together. I enjoyed seeing the working group, joined by renowned TB vaccine specialists from all over the world, work together so well.”

Within WHO and the Stop TB Partnership, recognition for the importance of new vaccines seems to have increased. Currently, only one vaccine against tuberculosis is available. The BCG vaccine protects thousands of children against severe forms of the disease but offers very limited protection against pulmonary TB in adults and adolescents. Safer and more effective vaccines could save millions of lives. Presenting a new vaccine strategy was certainly an important happening and the Working Group’s chair was happy to receive wide support for it. The Second Global Forum on TB Vaccines that was held in September 2010 in Estonia was another important happening. Mr Greco explains: “The Forum generated huge attention and we had significant success in improving cooperation between organisations. We also made important steps there toward the Blueprint for TB Vaccines.” The Blueprint is a document that describes the route to new vaccines and forms a strategy with which to achieve that goal.



Presenting it, in early 2012, is one of the things Mr Greco looks forward to most. “The Blueprint should also fuel more and better communications. Since we have been coordinating and working together more, we have gained more attention for the need for vaccines. That has also attracted attention from the pharmaceutical industry.”

Increased awareness is vital to Michel Greco. “Tuberculosis has always been considered a disease of the past, but it’s a disease of today. TB is everywhere, even in Europe. There are links with poverty, yes, but we also have the problem of drug resistance. That makes the case for vaccines.” According to Mr Greco, TB was not really an exciting subject and one that has been difficult to gain attention for. “But we are making progress.”



The Global Forum was important to Mr Greco for another reason. It was co-organised by TBVI, based in Europe, and Areas, based in the USA. Both organisations are working hard to find new vaccines against TB and the two have been tightening their relationship throughout 2010. Mr Greco is happy about the collaboration between the two organisations. “TBVI is now a balanced partner to Aeras and we all look forward to seeing the alliance crystallise and strengthen.”

“I’ll be the happiest man on earth if we manage to deliver a vaccine within ten years. But 2020 does seem possible.”

All this collaboration and communication should, of course, eventually lead to those much-needed new vaccines. The current vaccine portfolio holds a significant number of candidate vaccines at the moment. These vaccines are in various stages of development and testing.

Why so many? Couldn’t we just choose one promising candidate and guide it through the different phases of clinical trials? Wouldn’t that save both money and time? To Michel Greco it is simple: “If we knew what worked, we would have done that a long time ago. The problem is that we don’t know which candidate will succeed. That’s why we can’t stop doing research, even if we already have promising candidates.” For similar reasons, Mr Greco finds it difficult to make predictions about the delivery date of a new vaccine. Down to earth and realistic, he does not make promises that cannot be fulfilled. Nevertheless, he is positive about the current progress. “Looking at the challenges we face, I’ll be the happiest man on earth if we manage to deliver a vaccine within ten years. But 2020 does seem possible; things have accelerated over the past years. Projects have moved on, that’s part of the progress. It has helped us to better understand the rationale.”



Michel Greco sees good progress in the field of advocacy. The chairman of the Working Group believes that, in the case of vaccine development, advocacy should mainly target governments, donors and decision makers. Getting those people to invest in new vaccines is a challenge that requires advocates to work together. “Ten years ago, awareness about the need for TB vaccines was close to nil. That has increased substantially, but it’s not yet sufficient. I think HIV/Aids and TB should work together. TB would benefit from that because HIV still gets attention more easily, but HIV/Aids would also benefit because TB is a leading killer in people infected with HIV.”



Bringing people together, accelerating progress



Bringing people together to exchange scientific information, create awareness and discuss the future of TB vaccine research. That is one of the important instruments TBVI uses to achieve its goals. Bringing people together stresses the importance of the subject and creates positive attitudes. Bringing people together motivates, helps in the decision-making process and facilitates the exchange of new ideas. With this in mind, TBVI organised and co-organised several meetings in 2010, each with its own purpose and outcome.

NEWTBAC project meeting, Switzerland

In February, the kick-off meeting of the EU-funded NEWTBAC project was held in Switzerland. Like its predecessor, TBVAC, the project enables 35 universities, research institutes and industry partners to further develop their most promising results and continue research into new TB vaccines. Tom Ottenhoff, Professor of Immunology at Leiden University Medical Centre: "Almost all the TBVAC partners wanted to join the NEWTBAC project and several new partners have joined too. It is a very inspirational consortium: a big group of laboratories working together as a very homogeneous, collaborative team of people." During a four day meeting, researchers presented their work in an open and encouraging atmosphere.

Erik Böttger, Professor of Microbiology at the University of Zurich, described a common goal: "We are here to solve a problem, not only to foster our own paths. In order to develop a promising TB vaccine, it is important to combine all the paths we have." Hazel Dockrell, Professor of Immunology at the London School of Hygiene and Tropical Medicine, is hopeful about the future: "I think in the next four years, together we are going to bring a lot of progress, building on the strong foundation from TBVAC."

Innovate to eliminate tuberculosis, Brussels

TBVI values co-organising meetings with other partners. Collaboration strengthens our message and allows access to a broader audience. On 24 March, World TB Day, TBVI together with several other NGOs organised a

symposium on the theme "Innovate to eliminate tuberculosis" at the European Parliament. The meeting, attended by politicians, experts, decision makers and activists, was held to raise awareness about TB and emphasise the development of new vaccines as an important solution.

"We are here to solve a problem, not only to foster our own paths."

Françoise Grossetête, Member of the European Parliament (MEP), stated: "The EU research framework programmes have widely demonstrated the ability of the EU to be at the forefront of discoveries in the field of immunisation. We cannot lose this achievement and decades of investment." According to Dr Jorge Sampaio, UN Special Envoy to Stop TB, the European Commission can take up a "much more active and assertive role in combating tuberculosis by initiating important policies, increasing TB research funding, and tackling drug-resistant forms of tuberculosis."

Catherine Guy-Quint, former MEP and chair of the meeting, noted a wide and urgent call for new tools to fight tuberculosis. "This objective can only be achieved with new vaccines, drugs for treatment and diagnostics. Europe is extremely well placed in the search for and discovery of new vaccines. However, it needs to translate years of research and discovery into globally accessible vaccines and diagnostics," she said.

International TB vaccine symposium, Spain

TBVI, the University of Zaragoza and Fundación Ramón Areces together organised the international symposium 'Research and development of new tuberculosis vaccines' on 3 and 4 June in Zaragoza, Spain. The symposium brought together European researchers, Spanish government officials and representatives of international organisations and pharmaceutical industries.

"Science is a mix of competition and collaboration, in which we all work to achieve to our goal of new vaccines," Professor Carlos Martin of the University of Zaragoza said in his speech. He estimated that at least 500 researchers in Europe are working on TB vaccines; an impressive figure.

"Public and political commitment are needed."

The development of new vaccines against TB is progressing in promising ways, was the conclusion of the symposium. However, there are strategic challenges to be considered. Jan Gheuens of the Bill & Melinda Gates Foundation mentioned some of them: "What will be the next generation of new vaccines? New antigens or a new approach to vaccines? What about the cost of progress, can we raise the funds for larger clinical studies?" He added that fundraising is "tough" and that not just greater awareness of the challenges is needed, but also public and political commitment.

2nd Global Forum on TB Vaccines, Estonia

TB vaccine researchers and stakeholders from around the world met from 21-24 September in Tallinn, Estonia for the 2nd Global Forum on TB Vaccines. They assessed a decade of progress in the search for more effective TB vaccines and charted a path forward to sustain the momentum over the next decade. More than 200 participants from 31 countries attended the meeting, organised by Aeras, TBVI and the Stop TB Partnership.

The good news was that since the First Global Forum in 2001, there have been a number of accomplishments. At the time of the first Forum, no vaccines had yet advanced to human trials. At the time of the second Forum, ten TB vaccines were undergoing clinical trials and trials of two more vaccines had been announced. Other innovative new developments include an assay development project to improve the assessment of vaccine efficacy.

Besides celebrating accomplishments, the international meeting examined the challenges. These vary from the scientific complexities of developing vaccines against a disease without predictive animal models and no known correlates of protection, to the accurate development of timeline projections based on lessons learned, clinical trial design and financial support in an increasingly difficult fundraising environment. The already long and complicated process of testing vaccines is made more challenging by a general lack of capacity for clinical trials worldwide.



Financial report TBVI office



Revenue in euros	2009	2010
EC	157,205	349,639
Bill & Melinda Gates Foundation	429,469	837,109
Interest	10,647	14,730
Total	597,321	1,201,478
Expenses in euros		
Vaccine Research Program	558,008	1,074,987
Support services	39,313	65,702
Total	597,321	1,140,689
Result		
	0	60,789
Net assets		
Beginning	0	14,738
End of year	14,738	17,797

The 2010 financial statements have been audited by PricewaterhouseCoopers accountants NV. In their auditors' report they expressed an unqualified opinion on these financial statements. The financial report as stated above has been derived from the financial statements 2010. Result was added to unrestricted programme funds. A full financial report is available upon request.

New resources mobilised in 2010

TBVI was grateful to see existing sponsors continue their support. 2010 also brought access to new funds. The European Commission is supporting the NEWTBVAC project (see page 17) with almost 12 million euros, a Framework 7 project for the period 2010-2013. The beneficiaries' own budgets related to this programme total an amount of 7.1 million euros. The Government of the Republic of Korea sponsored the three Korean partners in this project with 560,000 euros over the same period.

Other new sponsorships were received from the Calouste Gulbenkian Foundation and GSK Biologicals. Fundación Ramón Areces and the Stop TB Partnership contributed in kind by co-organising a symposium. The total amount generated by these sponsorships is almost 200,000 euros.

Organisation (1 April 2011)



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**The Global Fund to Fight AIDS, Tuberculosis and Malaria
(GFATM), Geneva, Switzerland**

TB Europe Coalition

NIH Tuberculosis Research Unit (TBRU), Cleveland, USA

NIH, Bethesda, USA

WHO, Geneva, Switzerland

Facts about TB



Tuberculosis killed a staggering total of 1.7 million people in 2009. That is 4,700 deaths a day, or one person dying every 18 seconds. Many millions more struggle with this disease which, apart from causing great human suffering, also hampers the development of countries and slows down economic growth. BCG, the only currently available vaccine, offers very limited protection against pulmonary TB and is not safe in children infected with HIV. TBVI is committed to facilitating the development of more effective and safer vaccines against tuberculosis.

Tuberculosis is contagious and spreads through the air. If not treated, each person with active TB can infect on average 10 to 15 people per year.

Around two billion people, or one third of the world's population, are estimated to be infected with the bacterium and are at risk of developing the disease. One in every 10 of those people will become sick with active TB in his or her lifetime. People living with HIV are at a much greater risk.

The disease mainly affects young adults in their most productive years. People in the prime of their lives, who because of the long, burdensome, complicated and possibly even fatal course of the disease, are often no longer able to support themselves and their families (financially or otherwise) or help build up the economy of their country.

TB is a leading killer among people living with HIV, which causes a weakened immune system.

There were 9.4 million new TB cases in 2009. Per capita, the global TB incidence rate is falling, but the rate of decline is very slow, at less than 1%.

Multidrug-resistant TB (MDR-TB) is a form of tuberculosis that does not respond to the standard treatments using first-line drugs. MDR-TB is present in virtually all countries in the world. There were an estimated 440,000 new MDR-TB cases in 2008 with three countries accounting for over 50% of all cases globally: China, India and the Russian Federation.

Extensively drug-resistant TB (XDR-TB) occurs when resistance to second-line drugs develops. It is extremely difficult to treat and cases have been confirmed in more than 58 countries.

In 2010, the largest WHO MDR-TB survey reported the highest rates ever of MDR-TB, with peaks of up to 28% of new TB cases in some settings in the former Soviet Union.

The increased mobility of the world's population, with more people travelling across borders, intensifies the spread of tuberculosis.

The global burden of TB is estimated at hundreds of billions of dollars every year. The annual economic loss is 0.52% of the world's gross national income.

Although poverty related and mostly affecting people in developing countries, tuberculosis is prevalent in all continents. The situation is becoming serious in Europe, is alarming in most of Africa and extremely worrisome in parts of Asia.

In the 27 European Union member states, there were 101,566 new cases of tuberculosis in 2009. 1732 of these cases were diagnosed as MDR-TB, most of them in Romania and the Baltic states with a total of 5,364 deaths. This does not include several thousand HIV patients who also died of TB. Treatment in the larger European region costs over €2 billion per year. The region is under specific threat of drug-resistant strains of tuberculosis, which are more expensive and difficult to treat.

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