New Horizons for Vaccine Research & Innovation Conference

Brussels, 12-13 March 2014

Report

Rapporteur: Victoria English
**Background**

Vaccines designed to prevent infectious diseases are one of the most cost-effective interventions in public health and have prevented illness and death from devastating diseases such as polio, smallpox, diphtheria, measles, mumps and rubella. Yet these diseases represent only some of the many illnesses that currently threaten human health. The European Commission conference, New Horizons for Vaccine Research and Innovation, which took place in Brussels on 12 to 13 March 2014, examined work that still needs to be done to develop effective vaccines for HIV/AIDS, malaria, and tuberculosis, as well as other current and future infectious diseases. It looked at this challenge in the context of supporting European competitiveness and the health-related industries. The focus of the meeting was on preventive, or prophylactic, vaccines and the particular challenges that they pose from a development and delivery point of view.

In the past, vaccines were developed by individual scientists following the empirical approach of first isolating, then inactivating, and later injecting disease-causing microorganisms into subjects. These very effective and comparatively simple vaccines have to be considered ‘low-hanging fruits’, compared to the complex challenges of developing vaccines against the infectious diseases for which this simple approach has not worked. Vaccines of the future will therefore have to incorporate many disciplines, and will need to be developed in partnerships. These are likely to be partnerships amongst scientists in the academic community, industry, and the not-for-profit sector. The next generation of vaccines will need to be developed in new partnerships and with innovations implemented all along the development cycle, including better understanding of the diseases. Prior to, and during and after development, they will need to be assessed against different economic criteria in determining their cost and benefit to society. The European Union Framework Programme for Research and Innovation, Horizon 2020, can help meet these challenges by creating new research and financing tools and fostering the creation of new partnerships for developing vaccines, and supporting the wider international effort to eradicate disease.
**Day 1: Wednesday 12 March 2014**

**Welcome and opening**

*Ruxandra Draghia-Akli*, Director, Health Research, Directorate General for Research and Innovation, European Commission

*Ingmar Hoerr*, CEO, CureVac GmbH, Germany

*Ruxandra Draghia-Akli*, director of health research at the European Commission, opened the meeting, with a review of the health impact of vaccines, noting that in four disease areas vaccination had resulted in an almost 100% reduction in the number of cases compared with an earlier peak period. The statistics showed that by 2006, successive vaccination with agents against diphtheria, acute and paralytic polio, and smallpox had brought the case load for these diseases to zero. In the meantime, reductions of more than 90% were recorded for cases of measles, mumps, pertussis, rubella and tetanus, compared with their earlier peak levels. The Commission would like to see the list of disease where eradication is possible, lengthened, she said. It is in this context that the EU is financially supporting projects to extend and deepen vaccine research. Over the past 11 years the Union has spent €50 million per year on vaccine R&D including projects under both Framework Programmes 6 and 7 (FP6 and FP7). The FP6 and FP7 budgets also fund the Innovative Medicines Initiative (IMI) and the European & Developing Countries Clinical Trials Partnerships (EDCTP). IMI supports non-competitive research in a unique public-private partnership, while EDCTP is a public-public partnership supporting clinical trials in sub-Saharan Africa.

Looking ahead, the union will continue to support vaccines under Horizon 2020, including successor programmes for the IMI and the EDCTP. Horizon 2020 will support the entire innovation chain for vaccines from basic research to close-to-market research. Disease prevention will be a priority. Some of the early opportunities are being directed at small and medium sized enterprises (SMEs), cooperative projects targeting vaccines against diseases such as tuberculosis and HIV, and global initiatives aimed at supporting infectious disease preparedness research. Among the SME topics will be research into the clinical validation of biomarkers.

Meanwhile, IMI2, the successor IMI programme, will support new vaccine research and innovation. Preparations for the launch of IMI2 are underway with the first calls expected in the summer, Dr Akli said.

At the European Commission’s ‘Innovation Convention’, which took place prior to the conference, the Commission awarded two million Euro as its first-ever innovation inducement prize to CureVac GmbH, an SME from Tübingen, Germany, which has developed a novel platform for prophylactic vaccines against infectious disease. Using proprietary methods, the company can produce vaccines against almost any infectious disease and deliver them without observing the cold chain. The vaccines are based on messenger RNA (mRNA) technology and are stable at any temperature which means that they are ideally suited for delivery to locations in the developing world. *Ingmar Hoerr*, the chief executive, explained that the mRNA molecules are modelled after those in nature and have been built with naturally occurring nucleotides. They do not require any immune-stimulating adjuvants. CureVac has built its own GMP manufacturing facility. Besides candidate vaccines for infectious disease, the company is also developing therapeutic vaccines for prostate and lung cancers, and adjuvants for use with other vaccines.
Session 1: Vaccine innovation: with people – for people

Chairs:  
Emilio Mordini, Director of the Centre for Science, Society and Citizenship, Italy  
Marie-Paule Kieny, Assistant Director-General, World Health Organization

Speakers:  
Mitchell Warren, Executive Director, AVAC, Global Advocacy for HIV prevention, USA  
Heidi Larson, Senior Lecturer, London School of Hygiene and Tropical Medicine, United Kingdom

Panellists:  
Johan Giesecke, Chief Scientist, European Centre for Disease Prevention and Control  
Žaneta Ozolina, Professor in Political Science, University of Latvia  
Roxana Rustomjee, Chief Specialist Scientist, Strategic Health Innovation Partnerships, Medical Research Council, South Africa  
John F. Ryan, Director (acting), Public Health, Directorate General for Health and Consumers, European Commission  
David Salisbury, Director, Immunisation, Department of Health, London, United Kingdom  
Angus Thomson, Vaccines Europe and Director Vaccination Policy & Advocacy, Sanofi Pasteur, France

The first session, Vaccine innovation: with people – for people, featured presentations about how to engage the public in discussions about current and future vaccines. It was chaired by Emilio Mordini, Director of the Centre for Science, Society and Citizenship in Italy, and Marie-Paule Kieny, Assistant Director-General of the World Health Organization.

Whilst progress has been made in developing vaccines for many infectious diseases, it still hasn’t been possible to achieve an effective HIV/AIDS vaccine despite many years of research. Mitchell Warren, executive director of AVAC, a global advocacy group for HIV prevention, told the meeting that it is essential to maintain public support for coordinated HIV vaccine research. This can be done through ‘informed community advocacy.’ This means translating complex science to members of the affected community, and communicating the needs of the community back to the scientists.

There are more than 20 AIDS vaccine trials ongoing around the world. About 10 different vaccine strategies are in various stages of development including candidate DNA vaccines, neutralising antibodies, and adenoviruses. The candidate vaccine with the best clinical record thus far is ALVAC/AIDSVAX, a combination vaccine based on HIV strains common in Thailand. This vaccine has been tested in a Phase 3 trial in Thailand involving more than 16,000 qualified volunteers. The results, reported in 2009, showed that the vaccine was safe and lowered the rate of HIV infection by 31.2% in a sub-group of patients compared with a placebo. The trial is the only evidence thus far of an AIDS vaccine working in infected people, Mr Warren said.

Since the trial ended, a group called the Pox-Protein Private Partnership has been formed to coordinate follow-up research. This has led to the start of two immunogenicity studies. The partnership is planning further clinical studies for 2016/17. Crucial to the follow-up will be getting support for the vaccine strategy from the affected populations, Mr Warren said.

Absent a vaccine, there is still a lot that can be done to bring down new HIV infections, which are currently running at about 2.3 million per
year. These measures include delivering proven tools against infection such as condoms (through awareness campaigns and improved access) and rolling out new prevention tools such as 1% tenofovir gel. Vaccines however are at the top of the list of long-term measures for ending the epidemic. This list also includes developing multipurpose prevention technologies and next-generation anti-retroviral therapies.

Heidi Larson, senior lecturer at the London School of Hygiene & Tropical Medicine, addressed the issue of risk perception as it relates to the use of vaccines. One of the features of preventive vaccination is that it targets healthy people. This means that the public’s willingness to take risks is lower than when they are sick and taking a medication to feel better, and their expectation of vaccine safety is very high. Dr Larson told the meeting that perceptions of vaccine risk on the part of the population are important to acknowledge and address. Perceptions of risk are not new. What is new is the power of the internet and social media to spread these perceptions globally. Social media has also allowed the creation of self-organising networks of like-minded people both locally and globally who can put pressure on governments to alter their vaccine policies. These public concerns can be heightened in countries where there is already a distrust of government. As a starting point, governments need to establish credibility by generating trust. Trust can only be generated by openness, and openness requires that officials recognise uncertainty, where uncertainty exists, Dr Larson said.

In a panel discussion that followed, delegates discussed strategies for communicating the public health benefits of vaccination, and the impact of the social media. The social networks can’t be ignored. Rather, the issue is how public health officials can communicate more effectively through these networks, said Žaneta Ozolina, professor of political science at the University of Latvia. In this connection, the coming into force of new internet domain names this year may be an opportunity for health authorities to set up a regulated site with information on vaccines. For example, the National Health Service in England carries educational material on its sites. These are regarded by many as reference sites, said a delegate.

Johan Giesecke of the European Centre for Disease Prevention and Control said the centre produces materials for the EU member states to use in explaining the benefits of vaccination. John F. Ryan of the European Commission noted that the Commission is working with the member states and the WHO to reinforce vaccination policy and disease prevention.

Generating trust in vaccine policy may, in fact, be a case of communicating the idea that vaccination is the norm rather than the exception. In the UK, there is evidence that members of the public have a high level of trust in their family doctors. Any communication about vaccination should be done through these trusted healthcare professionals, said David Salisbury, former director of immunisation at the UK Department of Health.

But when physicians express doubts about vaccines, should they not be sanctioned, said a delegate from the Netherlands. She cited a high-profile case of a doctor who had been fined for opposing influenza vaccination. This generated scepticism amongst patients about the motives of the government.

In South Africa, there is considerable home-grown vaccine research against both tuberculosis and HIV which is generating funding from both the government and international charities. There is also a government-supported initiative to roll out the human papillomavirus (HPV) vaccine to nine and ten year old girls. Both the research and immunisation strategies are worked out in consultation with patient advocates. This has helped support vaccination policy, said Roxana Rustomjee, chief specialist scientist at the Medical Research Council, South Africa.

Angus Thomson of Sanofi Pasteur and Vaccines Europe observed that the only way to sustain support for vaccination is through multi-sectorial partnerships which engage in public conversation. The VaccinesToday.eu portal is a good example of transparent and open dialogue with concerned individuals, but successful initiatives like this need broader partnership and support from the public health community.
The second session, *Innovation in vaccine design*, featured a discussion of some of the newest vaccine technologies and how they can be developed and delivered. The session was chaired by Penny Heaton, Director of Vaccine Development at The Bill and Melinda Gates Foundation and David Salisbury, former Director of Immunisation at the UK Department of Health.

Rino Rappuoli, global head of vaccine research at Novartis Vaccines and Diagnostics, said the industry is sitting on the cusp of several new vaccine technologies that will transform the way healthcare is delivered. Whereas the earliest vaccines were developed by individual scientists following the empirical approach of first isolating, then inactivating, and later injecting the disease-causing microorganism into subjects, the newest technologies incorporate genomics and other modern disciplines. Since 1980, scientists have developed new agents using recombinant DNA technology; glycoconjugation; and reverse vaccinology to prevent diseases such as hepatitis B, *S. aureus* and meningococcal B infection. The new agent for MenB infection (Bexsero) was developed through reverse vaccinology, which involves screening the genome of the pathogen to discover target antigens.

The latest technologies include synthetic biology, structural vaccinology, and new methods for producing adjuvants. The MF59 adjuvant, for example, has been shown to increase the efficacy of influenza vaccines in children to 86% from 43%.

Structural vaccinology, also known as structure-based antigen design, describes a way of engineering antigens to make them more stable for use in vaccines. Recently, scientists have succeeded in analysing the structure of the respiratory syncytial virus (RSV) F protein and to use the information to design an effective vaccine antigen. Similarly, synthetic biology, which involves the design and construction of biological systems, has enabled the creation of synthetic influenza virus seeds against a pandemic strain in only 5 days. Most importantly, the seeds were
created in the laboratory using the sequence information that had been posted on the internet in China without the lengthy and dangerous process of shipping live viruses. Finally, systems biology is an inter-disciplinary approach for studying biological systems. When applied to clinical trials, it could help developers obtain more information from fewer subjects. In short, it could help execute smaller trials targeted at different groups such as children, pregnant women, adults, and the elderly.

Whereas in the past, the empirical approach produced successful vaccines, the agents of the future will likely require a collaborative approach involving experts in human immunology, systems biology, and epidemiology, Dr Rappuoli said. An example of this approach is the FP7 ADITEC project which has brought together 42 partners.

Else Marie Agger, director of infectious disease immunology at the Statens Serum Institut in Denmark, explained how adjuvants have advanced. Previously consisting of aluminium salts, the current and prospective agents offer a range of therapeutic benefits. These potential benefits include dose sparing and rapid response to pathogens. Adjuvants now in development might be suitable for use with new T cell vaccines to stop viral and bacterial infection, or with therapeutic vaccines to treat cancer. There are now many clinical studies involving adjuvants with different profiles including GLA-SE, an agent that would enhance T cell responses to influenza vaccines in older adults. Examples of adjuvants that have been approved for human use include virosomes, MF59 (Novartis), and two adjuvants produced by GlaxoSmithKline Plc (AS03 and AS04). In future, researchers will be looking at how adjuvants can help obtain tissue-specific responses from vaccines. With clinical work in novel adjuvants accelerating, there is a need to do head-to-head comparisons among the different agents, Dr Agger said.

Professor Giuseppe Pantaleo, executive director of the Swiss Vaccine Research Institute, told the meeting that the biggest disease targets such as tuberculosis, malaria and HIV require a more rational approach to vaccine development. One way to achieve this is to develop and validate biomarkers for safety and efficacy. A biomarker is defined as a biochemical feature or facet that can be used to measure the progress of a disease, or the effects of a treatment on a disease. Biomarkers indicate a current biological state, or they can point to a likely future state. In vaccine development, they are currently being explored as indicators of safety. For example, a five-year Innovative Medicines Initiative project, BioVacSafe (Biomarkers for Enhanced Vaccine Safety), is currently developing tools to speed the testing of vaccine safety, both before and after a product’s launch onto a market. This includes identifying and validating biomarkers of early inflammation and allergic response, as well as biomarkers of autoimmunity. Looking ahead, BioVacSafe could be used as a model for a similar initiative that would bring experts together to identify and validate early biomarkers of efficacy, Professor Pantaleo said. Such an initiative could use systems biology as a research approach.

Philippe Sansonetti, director of the molecular microbial pathogenesis unit at Institut Pasteur, talked about the need to develop vaccines for enteric infections which are still a major cause of death in children under the age of five years in developing countries. The infections include Shigella and Enterotoxigenic Escherichia coli (ETEC), both gram-negative bacteria that can cause diarrhoea. Because so many people are at risk from infection, including young children, refugees, and travellers, priority needs to be placed on developing a combination Shigella-ETEC vaccine, he said. But key issues remain to be resolved when testing live oral vaccines in children in endemic areas. These include whether similar formulations and doses can be used in all groups and settings, and whether they can be safely administered to HIV-infected children. These, and other issues, are being investigated in the EU project STOPENTERICS, which is funded under the Seventh Framework Programme (FP7). The project started in 2010 and will run for five years. It is looking to identify novel antigens and generate novel vaccine formulations, as well as develop cell-based and animal models to evaluate candidate vaccines for human trials.

One of the biggest global health threats is tuberculosis. Session Chair Penny Heaton
presented the slides of **Thomas Evans**, President and Chief Executive of AERAS, who was not able to attend the meeting. AREAS is a non-profit enterprise which is developing TB vaccines. TB is an airborne infection that causes nearly 8.5 million cases of illness each year. The disease also kills one in four people infected with HIV. The goal of public health authorities is to reduce the number of cases to fewer than one million per year by 2050. To reach this target however, scientists will have to generate and apply some transformational interventions. These include preventing the transmission of the bacterium, blocking its progression to an infectious state, and treating and sterilizing active TB. At the moment, scientists don’t fully understand how TB is transmitted, and the differences in transmission based on current strains. Nor do they understand why some people relapse after treatment. Moreover if someone is infected with TB, what causes the disease to progress? A new vaccine that could prevent adolescents and adults from developing and transmitting TB would be the single most cost-effective tool in mitigating the epidemic, Dr Evans said. Even a 60% efficacious adolescent and adult vaccine, delivered to 20% of the target population could potentially avert 30 to 50 million incident cases of TB by 2050, he added. The global pipeline of TB vaccine candidates currently includes one Phase 3 vaccine candidate; eight candidates in Phase 2 and four in Phase 1. A currently marketed vaccine, Bacille Calmette-Guérin (BCG), is used in many countries with a high prevalence of the disease, but it is not wholly protective.

**Adrian Hill**, director of the Jenner Institute at the University of Oxford, spoke of the need to rethink clinical trial design in order to speed up the development of vaccines for HIV/AIDS, malaria and tuberculosis. It takes too long to bring new agents onto the market as illustrated by the 20-year clinical development time for RTS,S, a prospective malaria vaccine developed by GlaxoSmithKline, he said. RTS,S will be submitted to the European Medicines Agency for review this year, decades after the first concept for the vaccine was elucidated. In order to speed up vaccine development, some people have suggested the use of adaptive trial designs and commercial incentives such as advance market commitments. However there is another route to faster development: experimental medicines studies, Dr Hill said. These are small-scale, rapid clinical studies that aim to test new concepts, compare vaccine types, search for efficacy signals, and identify biomarkers of efficacy. These trials might be biopsy studies in HIV to discover how scientists can induce mucosal immunity; prime-boost studies in malaria to find out whether CD8+ T cells protect humans; and aerosol immunisation in TB to discover if new routes of immunisation will help prevent the disease. Such studies could also discover the most useful adjuvants as well as the best antigens from complex pathogens. Other ways to save time and money would be to review biomanufacturing regulations for small trials, support open access to adjuvants and vectors, and continue to support trials in developing countries.

Are regulatory issues a major bottleneck for vaccines? **Brigitte Keller-Stanislawski**, head of the safety of medicinal products and devices at the Paul-Ehrlich-Institut, addressed this question in a summary of the regulatory requirements for vaccine development. Vaccines, she pointed out, are different from other medicines because they are usually given to healthy people. As a consequence, the public has a low tolerance for adverse events. There are four marketing authorisation procedures in Europe: the national, mutual recognition, and decentralised procedures, and the centralised procedure at the European Medicines Agency. Developers have some flexibility in their choice of procedure unless the agent is a biologic or targets a high-impact disease like AIDS, in which case the centralised procedure is mandatory. Under both the centralised and decentralised procedures, the assessment time is a maximum 210 days. What is new is the requirement that developers of vaccines and other products submit risk management plans with their marketing authorisation applications. These plans are meant to identify potential problems before they become adverse events. In the case of vaccines, it might mean identifying potential toxicities in adjuvants, or possible viral shedding from live attenuated vaccines. Or it might mean being aware of how changes to a manufacturing process could affect safety and efficacy.

In the **panel discussion** that followed the second session, delegates reiterated the idea
that vaccine discovery and development has moved from the one-man empirical approach, to a network science involving many people with different disciplines. Having said this, there is still a need to identify incentives that will draw people together. Penny Heaton described this task as identifying the ‘edges’ of research where collaboration becomes more beneficial to all the parties than competition. Rino Rappuoli said people need to ‘gain something’ in order to be part of a collaborative project.

The value of early head-to-head studies of vaccine candidates was highlighted. More comparative studies will enable developers to establish criteria for success. This in turn becomes an incentive for developers to work together. Moreover, working on new science is itself an incentive. Else Marie Agger said that ‘the passion of scientists’ isn’t any different if they are working on their own project or someone else’s. Giuseppe Pantaleo noted that if there were to be more head-to-head studies then developers would need to have access to a central facility.

Delegates also discussed ways of overcoming bottlenecks in vaccine development. This could include checking early-development procedures for redundancies. There could, for example, be heretofore unidentified bottlenecks in chemistry, manufacturing and control (CMC) procedures. Measures that might speed progress include sharing antigens and/or adjuvants among companies; selecting the best assays and animal models to test vaccine efficacy; and developing reference standards so that experiments can be compared with one another.

Current regulatory requirements were also discussed1. Adrian Hill noted that regulations might be adapted to allow for the running of small experimental studies to identify the best candidate vaccines more quickly. For example, such trials might test a candidate vaccine with three different adjuvants. Rino Rappuoli noted that systems biology could help extract the best information from small trials. Vaccine research could also benefit from a wider use of patient registries. Regarding outcomes, there was some discussion about whether expectations for the success of some vaccine candidates, such as those for tuberculosis, might be too high. In the case of TB, many people might still benefit from a new vaccine of ‘modest efficacy,’ it was noted.

A delegate from GlaxoSmithKline called for a ‘reflection’ on the R&D model for vaccines. This would involve considering an ‘adaptive licensing’ approach, where candidate vaccines that have achieved proof-of-concept could be administered early to subjects in a controlled real-life setting.

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In the opening address on the second day of the conference European Commissioner for Research, Innovation and Science Máire Geoghegan-Quinn said the Commission will be stepping up its investment in vaccine research under Horizon 2020, the new EU programme for research and innovation. More than €7 billion is being allocated to the programme’s ‘Societal Challenge 1’, Health, Demographic Change and Wellbeing. Within this, vaccine research will play a prominent role. The Horizon budget will also support successor projects for the Innovative Medicines Initiative (IMI), a public-private partnership, and the European and Developing Countries Clinical Trials Partnership (EDCTP), a public-public partnership. IMI2 is expected to fund research into the entire value chain of vaccine research, while EDCTP2 will continue to conduct clinical trials of vaccines in sub-Saharan Africa.

In a further step, the Commission is working with the Bill and Melinda Gates Foundation, in collaboration with the European Investment Bank, the EDCTP, the Tuberculosis Vaccine Initiative, AERAS, partners from the most affected countries, and other actors worldwide to develop a Global TB Vaccine Partnership. The Commission is looking to engage other partners in this effort. The aim is to speed up TB vaccine development through collaboration. The concept is that if everyone can be brought to the table together, it will be possible to make more informed choices on which new vaccine candidates are the most promising for further development. In support of this initiative, the Commission is allocating €25 million to TB vaccine development under Horizon 2020. It is also considering innovative financing mechanisms for late-stage TB vaccine trials. Commissioner Geoghegan-Quinn said vaccine development wouldn’t be complete without considering the role of animal health. Rabies is one example where the vaccination of animals can prevent disease in humans. There are many other examples where research on animal and on human vaccines should be done together, rather than separately, she noted.
The third and final session, Vaccine innovation – who pays? was chaired by Magdalena Rodríguez de Azero, Executive Director of Vaccines Europe, and Marja Esveld, senior adviser for research and innovation at the Ministry of Health, Welfare and Sport in the Netherlands.

The traditional childhood vaccines (EPI vaccines) are one of the most cost-effective interventions in public health. But newer vaccines have been more costly, Mark Jit, senior scientist at Public Health England, told the meeting that both the direct and indirect benefits of vaccination can be factored into future economic analyses of these vaccines. Cost-effectiveness analysis traditionally looked at the incremental cost of introducing a vaccine divided by its incremental benefit. This gave measurable outcomes such as cost per life years or quality-adjusted life years saved through vaccination. Direct costs of vaccination include the price of the vaccine plus the cost of administration. But indirect costs are also important in many situations. These can include the cost to society of lost productivity from disease. Another consideration is equity in the health and economic impact of vaccination. Hence an important consideration is whether all members of society, particularly people who are least well-off or who have the highest burden, can benefit equally from vaccination. New economic models are being developed to incorporate the wider costs and benefits of vaccination, Dr Jit said.

Gerald Voss of GSK Vaccines gave an industry perspective on the cost and benefit of developing new vaccines. At the onset of a new development program a fundamental consideration should be weighing up the overall development risk versus the potential return. Before initiating a new development program, a company like GSK will define the overall value proposition of a new vaccine and translate the related vaccine attributes into a Target Product Profile. The ultimate goal being successful registration with regulatory authorities, recommendation for use from public health advisory committees and reimbursement by payers.

Given the significant time and financial investment, the challenges for developing new vaccines can be very substantial, in particular if the targeted disease is complex and/or affects particular populations (immune-compromised, others). In order to overcome those challenges, two principles will enable sustainable vaccine development in the future: innovation and partnership. Innovation needs
to happen across the development cycle by, among other things, finding new antigens and adjuvants, managing clinical trials efficiently, or introducing adaptive regulatory pathways. With the ever increasing complexity and challenges of vaccine development, the concept of partnerships becomes essential. Partnerships enable a joint effort to develop new vaccines by pooling towards a common goal complementary skills, experience and resources from different players. This is particularly relevant for vaccines that tackle diseases that predominantly affect the Developing World.

As an introduction to ‘Cooperation and partnerships to improve vaccine R&D’, Line Matthiessen, head of the unit ‘Fighting infectious diseases and global epidemics’ at the European Commission, outlined the funding landscape for vaccine research and innovation under Horizon 2020. She also presented some of the call topics relevant for vaccine research published as part of the first Horizon 2020 work programme: In 2014/2015 two call topics focus on vaccine development for tuberculosis and HIV respectively. Throughout, priority will also be placed on training the next generation of scientists as well as supporting SMEs. She also explained how information about upcoming calls can be accessed online.

Product development partnerships (PDPs) were discussed by Odile Leroy, executive director of the European Vaccine Initiative (EVI), and Hansi Dean, director of new alliances at the International AIDS Vaccine Initiative (IAVI). PDPs are non-profit organizations that facilitate partnerships of public and private organizations to address public health needs for which the perceived commercial market is small. Dr Leroy explained that EVI, which is government-funded, addresses the ‘translation gap’ in vaccine development for diseases of poverty. It does this by supporting clinical studies up to Phase 2 for candidate vaccines mostly targeting malaria. Its portfolio currently includes 31 malaria antigens in 29 vaccine formulations, three of which are specifically aimed at preventing malaria in pregnant women. In progressing this portfolio, the EVI is partnered with 46 public institutions, 10 of which are in Africa, and with 19 private companies. EVI also participates in (and in many cases coordinates) a number of projects funded by the European Commission and EDCTP. Similarly, IAVI is a not-for-profit organisation supported by foundations, governments and companies. IAVI’s goal is to ensure the development of vaccines to prevent HIV infection. It is doing this through R&S and regional partnerships with academic institutions and industry to bridge basic HIV vaccine research to advanced product development. IAVI conducts internal R&D projects as well as advancing partnered vaccine candidates to product development, in collaboration with African clinical research centres.

The biggest public-private partnership in research to date is the IMI which is a partnership between the European Commission and the European Federation of Pharmaceutical Industries and Associations, EFPIA. Michel Goldman, the executive director, explained that IMI projects are supported by in-kind contributions from EFPIA and a cash contribution from the European Commission’s Framework Programmes for Research and Innovation. The public participants in IMI projects are usually a mixture of academic groups, hospitals, small and medium-sized enterprises, patient organisations and regulators. The projects address research topics relevant to both sides. An example is the ADVANCE project which aims to establish best practice for the assessment of the risk-benefit profile of vaccines. Vaccines will play a prominent role in IMI2, he said.

The European and Developing Countries Clinical Trials Partnership or EDCTP, is a public-public partnership, financially supported by 16 European countries and the European Commission. Its goal is to conduct clinical trials of new or improved medical interventions for HIV/AIDS, tuberculosis, and malaria in partnership with 49 countries in sub-Saharan Africa. The organisation is now moving into a second phase where the mandate will be extended to include clinical trials for other neglected infectious diseases, Ole Olesen of the EDCTP told the meeting.

Financing innovation is one of the missions of the European Investment Bank, the EU’s long-term lending institution. Shiva Dustdar, Head of RDI Advisory of the EIB told the meeting
that the Bank and the Commission will jointly commit risk capital to SMEs, corporations, and public research institutions in the context of the financial instruments under the Horizon 2020. The EIB’s RDI Advisory Services are currently reviewing various options to further enhance the support for the vaccine ‘ecosystem’ in Europe.

While Europe works on improving its vaccine infrastructure, the developing world hasn’t been standing still. Suresh Jadhav, executive director of the Serum Institute of India Ltd, said that 37 enterprises in 14 countries are now members of the Developing Countries Vaccine Manufacturers Network which produces vaccines for agencies of the United Nations. In 2012 the network accounted for 50% of the procurement volumes of UNICEF. At the same time, the manufacturers have largely kept the prices of traditional childhood vaccines affordable. This comes at a time when ‘Big Pharma’ is showing a reduced interest in supplying traditional vaccines to the developing world. Partnerships and funding from international agencies such as the WHO have made it possible for indigenous companies to create manufacturing capacity in the developing world, he said.

**Final panel discussion**

In a panel discussion after the final session, delegates debated how vaccine development could be made more sustainable. Partnerships such as IAVI and AERAS have enabled new research by virtue of shared funding and a pooling of expertise. These partnerships can accomplish things that a single company would be unable to do, said a delegate. At the same time, countries in the developing world have also built R&D and manufacturing capacity. Can Europe stay competitive? A lot will depend on regulation; whether the regulatory pathway is easy to navigate or burdensome, this delegate said. Others argued that Europe is indeed ‘on the right track’ with its focus on supporting new technologies and vaccinating populations at risk, including most recently the elderly. There is also institutional support in Europe for SMEs which are helping bring new vaccines forward in the absence of major efforts by ‘Big Pharma’. Meanwhile the European Investment bank is supporting SMEs through its risk-sharing financing facility. The bank also partners with commercial banks to make sure that there is a continuous flow of private funds to these companies, the EIB representative said.

On the subject of funding, delegates said the challenge is not just attracting new money but using existing funding better. This means reviewing the way clinical trials are conducted, re-evaluating the management of intellectual property, making progress towards collaborative ‘portfolio management’ of vaccine candidates, and taking advantage of virtual research networks.
Conclusions and recommendations

Panelists: Chairs from all sessions

Ruxandra Draghia-Akli, Director, Health Research, Directorate General for Research and Innovation, European Commission

Moderator: Zulfikar Abbany, Journalist, Deutsche Welle, Germany

- Future vaccine trials need to be adapted to the ageing population;
- Public health officials need to engage with people who are hesitant about vaccine use and be mindful of the power of the social media to spread misinformation;
- Public health officials shouldn’t reject social networks but should learn how to use them more effectively;
- The experience of South Africa illustrates the importance of having patient advocates to help roll out new vaccines;
- Public health authorities need different strategies to address the three types of people who have doubts about vaccines: the well-educated; religious objectors; and the underserviced who mistrust the state;
- In the past, vaccines were developed empirically by single scientists; today and in the future, vaccine development will require partnerships and more systematic approaches;
- Vaccine developers need to accelerate the clinical evaluation of novel adjuvants as well as do head-to-head studies of adjuvants;
- Biomarkers of both vaccine safety and efficacy need to be developed;
- Developers need to identify potential bottlenecks in manufacturing and in chemistry, manufacturing and control (CMC);
- The development of new vaccines needs to exploit the potential of exploratory, small-scale ‘experimental medicine’ trials for candidate adjuvants and vaccines. These trials could obtain a maximum of biological information from a limited number of patients in a comparatively short time. This information could guide the optimisation of the vaccine candidate, the dosing schedule, and the adjuvant. This could inform larger and more expensive trials;
- Social scientists should be involved in vaccine research and development;
- Economic evaluation of vaccines is key to evidence-based decision taking, such evaluations may consider a wide range of outcomes such as equity and productivity costs;
- Immunological assays need to be standardised;
- The European Investment Bank needs to consider how it can support the vaccine market as a whole;
- ‘Portfolio management’ approaches for the selection of vaccine candidates at different stages of development need to be optimised, in particular among public funders and within product-development partnerships;
- The IP management of vaccine companies needs to be adapted to facilitate collaboration at an early stage of product development; and
- Product development partnerships working on the research and development of most needed vaccines, globally, are efficient in filling critical gaps on the development continuum. This and other product development partnership models need to be supported and further expanded.