Year 1 Impact Assessment

February 2013

BACKGROUND

In support of Deliverable 19.1, "*Impact assessment done through impact score card throughout the project",* a score card was drafted by a small Steering Committee subgroup with support of the project manager incorporating the key areas identified in Work Package 19. Feedback was sought from an external expert consultant and was incorporated. This draft, along with a set of definitional guidelines for each of the 34 identified data elements, was circulated to all consortium partners in the final month of project period one. Project impact during the first project was assessed and impact will continue to be assessed for the duration of the project. Responses were received by 93% of project participants and incorporated into this 2012 Impact Assessment Report.

INTRODUCTION

The science behind vaccines has become so sophisticated that no one laboratory can tackle modern vaccine science in isolation. Therefore some of the most competitive European research groups from public institutions and biotechs, together with top US groups on systems biology and adjuvants, have agreed to join forces in the Advanced Immunization Technologies ADITEC consortium. The ADITEC project is a 30M High Impact project funded by the European Commission. The scope of the project is to accelerate the development of novel and powerful immunization technologies for the next generation of human vaccines. This goal requires a multidisciplinary approach in which diverse but complementary scientific disciplines and technologies converge.

The research consortia participating in the ADITEC project consist of:

- large biopharmaceutical companies
- small- and medium-sized enterprises
- universities
- independent research institutes
- hospitals
- regulatory agencies

Several ADITEC scientists and institutions are part of the Sclavo Vaccine Association (SVA), the coordinating institution, which is dedicated to vaccine research and development.

The working concept of ADITEC is to use systems biology and advanced immune assays to elucidate, at a highly sophisticated level, to learn more about how effective vaccines stimulate the human immune system and then to apply this information to the rational design of novel and highly targeted immunization technologies against vaccine-resistant pathogens.

Over the five year duration of the ADITEC project, impact will be seen in the areas of innovation, knowledge, European competitiveness, public health in targeted sub population groups and in the structuring of the European Research Area (ERA) in the field of vaccine research. The first project year is complete and impact is already evident. However, future years will bring an increased level of impact in all of these areas as the consortium and its research matures.

NEW BIOMEDICAL PRODUCTS, CLINICAL METHODS, VACCINATION DEVICES, ROUTES AND TIME SCHEMES FOR ADVANCED VACCINATION TECHNOLOGIES.

ADITEC is generating new knowledge on the human immune response to vaccines with a range of innovative vaccine technologies, to design new preventive or therapeutic immunisation strategies that will impact on prevention, alleviation or cure of disease.

The partners of ADITEC have begun to tackle the development of different prototype and innovative second generation adjuvants, modulators and delivery systems, innovative live antigen delivery vector systems and new

vaccine formulation and delivery devices. ADITEC has begun the evaluation of different routes of immunization for a range of well-defined antigens, formulations and delivery devices or vectors to provide information on the magnitude and quality of the immune response in different anatomical sites. The evaluation of differing immunization schemes, in particular heterologous prime-boost approaches to provide information on the immune responses at different anatomical sites has also been initiated. Specific prime-boost approaches combined with specific immunization routes are being comparatively evaluated and will allow an informed decision on selection on their use for new preventive or therapeutic vaccines for specific diseases.

Impact

In this early stage of the ADITEC project, **one patent** related to expression systems comprising polynucleotides encoding proteins and useful in the treatment of infections, has already been filed and published by Partner 29 (Okairos).

In addition to the successful patent, new adjuvants Partners 31, and 21 (Vaccibody, and King's College London) have each identified while Partner 5 (Institute Pasteur) has identified a new vector allowing the delivery of ESX antigens into airway dendritic cells In total, **eight advanced immunization technologies** have been identified.

Clinical trial work is well underway and will begin to produce significant results in the coming grant periods. **Twelve clinical trials** are planned, of those five are in the protocol development stage and four have been initiated. The four initiated studies are: i) Trivalent inactivated vs MF59 adjuvanted influenza vaccine in 14 -26 month healthy children (Phase IV), ii) menB - adjuvants shaping immune response (Phase I/II), iii) Tick-borne encephalitis – targeted immunisation (Phase IV), iv) Cholera & flu - comparison of sublingual and intranasal routes of immunization (Phase IV). The clinical study of *S. sonnei* vaccine (Ss-OAg-GMMA), was selected as first Phase I clinical trial with novel technology.

WP	Partners	Title of Trial	Phase	Status	Due date (M)
7	15- OEAW	HBV in elderly	IV	Protocol development	48
7	6-UOXF 8-UNIGE 9-NVD 13-EMORY	Trivalent inactivated vs MF59 adjuvanted influenza vaccine in 14 -26 month healthy children	IV	Initiated	48
7	15-OEAW 9-NVD 10-ICLL	H5N1 + IC31 adjuvant in elderly	II	Strategic Planning	54
10	43-SURREY	HBV - adjuvants systems biology	IV	Protocol development	48
10	43-SURREY 7-UNISI	Influenza - heterologous prime-boost	IV	Protocol development	48
10	9-NVD	menB - adjuvants shaping immune response	I/II	Initiated	48
11	43-SURREY	Tick-borne encephalitis - targeted immunisation	IV	Initiated	48
11	11-UGOT	Cholera & flu SL-IN	IV	Initiated	48
12	6-UOXF 39-NVGH	Typhoid vaccine & challenge	I/II	Protocol development	60
13	39-NVGH 43-SURREY	Trial 1: Shigella - novel antigen, routes, device	I	Protocol development	36
13	-	Trial 2 - adjuvants or other	I/IV	Open Call	48
13	-	Trial 3	I	-	60

BOOSTING EXCELLENCE OF EUROPEAN VACCINE RESEARCH LEADING TO MORE AND BETTER GENERIC KNOWLEDGE NEEDED TO SUPPORT VACCINE DEVELOPMENT

Broader impact in European vaccine research will be accomplished by stimulating interaction and cooperation among scientists by facilitating the exchange of information on the progress of current projects, participation in scientific meetings, and publication of scientific papers. Beyond the scientific research community, impact will be made through building awareness about the ADITEC project, objectives, the need for better optimized vaccine enabling technologies to fight infectious diseases and the scientific progress.

Specifically supporting vaccine development, generic knowledge in the areas of preclinical models which assess safety and efficacy, as well as age related effects will be shared and will provide preclinical proof of concept for selected new preventive and therapeutic vaccine strategies. These studies will allow informed decisions on the use of these selected strategies for further non-clinical and clinical studies.

Systems biology approaches will be employed to understand how effective vaccines stimulate the human immune system. By employment of advanced systems biology approaches combined with state-of-the-art imaging as well as immunological assays, ADITEC partners will identify molecular signatures that correlate with, and predict, various key parameters of the innate and adaptive immune response. In addition, insights into the molecular mechanisms driving innate and adaptive responses to vaccination will be gained and shared with the vaccine development community.

Impact

Year 1 of the ADITEC project has produced and disseminated a surprising amount of knowledge for only the first year of the project.. **Nineteen publications** have appeared in peer reviewed journals. Four of these publications were authored jointly between two or more ADITEC partners. The articles were published peer reviewed journals with impact factors ranging from 2.731 to 23.268. Three publications have factors over 10 and seven between 5-10. The partners have identified **13 exploitable results** from work completed to date. The number of publications and exploitable results will grow as the project progresses.

ADITEC Publications: Journal Impact Factors

Nature Biotechnology (1)	23.268
Nature Reviews: Microbiology (1)	21.182
Journal of Experimental Medicine (2)	13.85
PNAS (1)	9.681
PloS Pathogens (1)	9.127
Trends in Microbiology (1)	7.910
Science Translational Medicine (1)	7.800
Current Opinion in Biotechnology (1)	7.711
Mucosal Immunology (1)	6.963
Retrovirology (1)	6.470
Journal of Biological Chemistry (1)	4.773
PloS one (2)	4.092
Microbial Cell Factories (2)	3.550
Tuberculosis (1)	3.474
Immunobiology (1)	3.205
International Journal of Tuberculosis and Lung Diseases (1)	2.731

Extensive active dissemination occurred though year one as ADITEC partners were invited to **12 international conferences**, made **56 conference presentations** and attended over **100 conferences**.

The ADITEC project kick-off meeting was organized and attended by **100 participants**. Several work package meetings were held through the year, along with seven Steering Committee meetings. The External Advisory Board met, and through a series of meetings, made a formal recommendation for the selection of the 3rd Model

antigen. All of these meetings focused on project status reporting, decision making and sharing of information among a wide variety of organizational representatives.

The project "kick-off" press release was carried by approximately **100 news sources** (print and websites). Additionally, ADITEC made entries in four blogs, published **2 newsletters,** mailed to **over 750 people**, and published **2 general articles** in journals creating a broad awareness of the project and its goals.

Scientifically, **five advanced animal models** have been developed by Partners 23, 5 and 42 (French Atomic Energy, Institute Pasteur, and Imperial College). Pre-clinical studies were conducted to identify correlates of protection comparing different routes of immunization, prime-boost strategies and the effect of age in response to vaccination. Animal models of challenge with influenza (ferrets), M. tuberculosis (mice and guinea pigs) and Chlamydia (mice) were established are ready to conduct protection studies with selected formulations.

In addition, Partners 2, 31, 21 and 32, (SSI, Vaccibody, King's College and Pevion) have reported the identification of **19 immunological signatures**.

REINFORCE THE EUROPEAN COMPETIVENESS THROUGH KNOWLEDGE EXPLOITATION BY EUROPEAN INDUSTRIES ACTIVE IN THE DEVELOPMENT OF VACCINES OR SUPPORTING PRODUCTS SUCH AS ADJUVANTS, VECTORS OR VACCINATION DEVICES.

The ADITEC project represents a very important model in public private partnerships (PPP) that could become a model for future initiatives. This approach was created because the required technologies and expertise are so varied and sophisticated that it could only be carried out if many different laboratories with overlapping excellence join together. The programme integrates the work of 42 partners from 13 countries. The involvement of a substantial number of European SMEs (13) and vaccine companies (2) in this field will result in a strongly enhanced and integrated exploitation by European industries. Their involvement and commitment with R&D activities are among the most competitive in the EU.

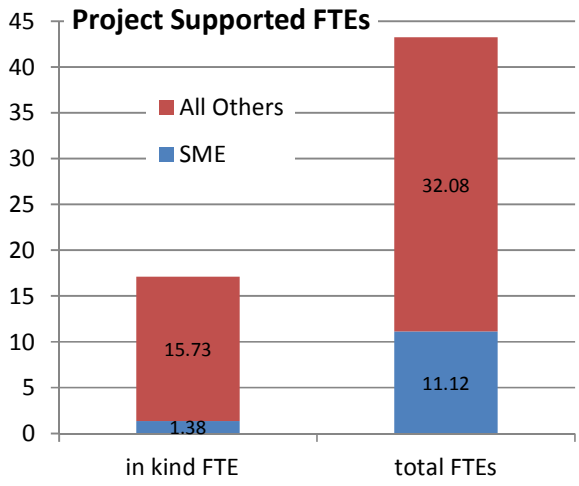
Internationally recognised training programmes cover targeted training in vaccinology at masters and professional levels, addressing both specific and broad aspects of translational immunology and vaccinology. The training will synergize with existing training schemes and support structures at Novartis Vaccines for Global Health and the University of Siena, the Advanced Course of Vaccinology (ADVAC) organized by University of Geneve and Fondation Merieux, translational vaccinology training at Surrey Clinical Research Cenetr, and training modules in adjuvant and vaccine formulation at WHO. These activities impact the European vaccine industry by mobilising these existing courses in a coordinated way and by promoting mobility and exchanges between participating EU countries and between academia and SME and industry institutions.

These joint training activities will provide another mechanism for bringing together the variety of project partners and also provide a vehicle to disseminate knowledge gained in the project. These approaches will facilitate the integration of research capacities, both public and private, across Europe and contribute to a wide dissemination of knowledge increasing European competitiveness.

Impact

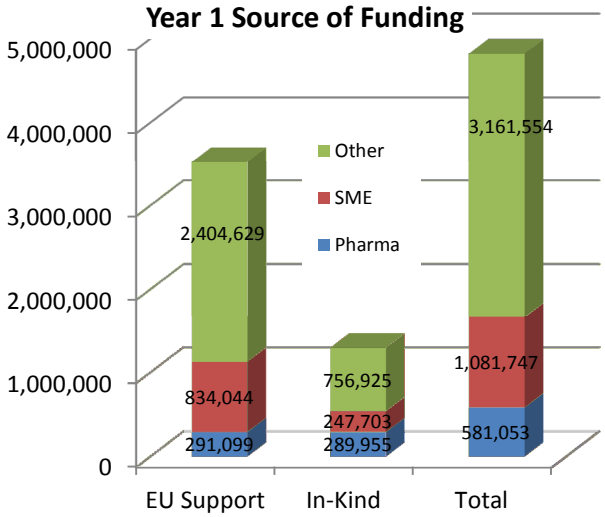
ADITEC members participated in the development and teaching of both the ADVAC course, as well as the Masters Programme in Vaccinology and Pharmaceutical Clinical. ADITEC sponsored **6 fellowships** for the Masters Programme**, 4 fellowships** in the ADVAC Course and will sponsor up to **12 fellowships** in the coming year. Training is also provided to Post docs/PhDs within the labs of partners. To date, **14.4 Post Doc/PHD FTEs** have been supported by ADITEC with 1 in the lab of an SME.

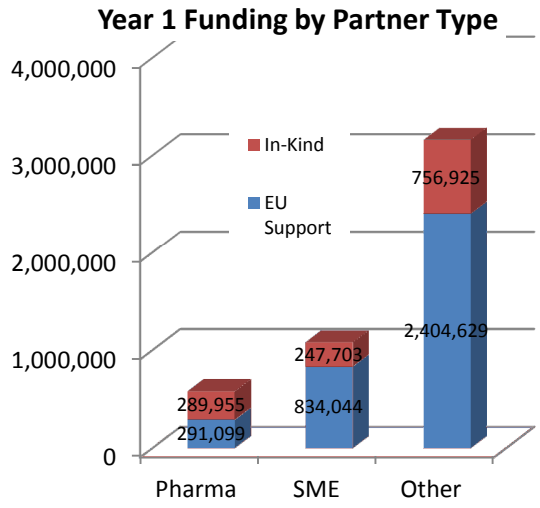
In total **43.2 FTEs** were reported receiving ADITEC support during the first project year, with 11.12 located in SMEs. The project received **17.11 FTEs of in-kind support**, with 1.38 FTEs coming from SMEs.



In Euro, the first year of the project was funded with a total of €4,824,355. Of this amount, €3,529,772 was European Commission support and €1,294,583 was in-kind donation. The expense distribution by type of organization is:

Total	Pharma	€ 581,053	SME	€ 1,081,747	Other	€ 3,161,554
EU Support	Pharma	€ 291,099	SME	€ 834,044	Other	€ 2,404,629
In-Kind	Pharma	€ 289,955	SME	€ 247,703	Other	€ 756,925





Partner 24 (CRNS) reported **€45.000 ERA funds leveraged** for vaccinology from the Euronanomed Research Program and Partner 23, (CEA) reported leveraging **330,000€.**

PUBLIC HEALTH ISSUES IN TERMS OF DIRECTING RESEARCH TOWARD VACCINES FOR THE VERY YOUNG AND THE ELDERLY

As a most effective public health measure, vaccines are developed to meet the needs of the largest part of the target population, be it healthy children or adults. However, most of the disease burden in Europe affects individuals who are vulnerable because of their age (very young or elderly) or their co-morbidities. These vulnerable populations, routinely excluded from industry-sponsored clinical trials, are consequently deprived of evidence-based recommendations and/or efficient vaccines. This is demonstrated by the lack of influenza vaccines licensed for use prior to 6 months of age or by the most limited efficacy of split and subunit influenza vaccines in young children, in adults with chronic diseases affecting their immune competence, and in older adults. Similarly, gender issues have long been recognized as key determinants of immune responses, but key questions remain unanswered. Lastly, vaccines have long been considered as a "one size fits all" public health intervention, whereas genetic factors are now demonstrated as exerting a most critical influence on the predisposition to both infectious diseases and vaccine responses. These host factors affect both primary and memory vaccine responses, severely limiting the short-term and long-term benefit of current vaccines and immunization strategies.

Impact

Preclinical studies are actively underway in both elderly and neonatal mice. **One human study**, Trivelent inactivated vs MF59 adjuvanted influenza vaccine in 14-26 month children has been initiated. **Two remaining human** studies, HBV in elderly is in the protocol development stage and the H5N1+IC31 adjuvant study in elderly is still in planning stages.

Mathematical models are currently being developed, and when data are available, will be used to assess age and gender related factors.

STRUCTURING THE EUROPEAN RESEARCH AREA IN THE FIELD OF VACCINE RESEARCH

In order to provide additional budget for innovative ideas and to advance promising candidate to the clinic and build other long term initiatives, an active dissemination, advocacy and resource mobilisation programme has begun. For this an extensive network of contacts with foundations, private funders, private industry, regional, national and European governments is being expanded to advocate for the impact on the economy, health, and competitiveness of the activities of this highly integrated programme, and to gain support for its co-funding and sustainability.

The Sclavo Vaccines Association is interfacing with other economic, industry and trade, health and developmental agencies of members and associated states national programmes. The association has developed links with other complementary partnerships and programmes in member states and associated members states in this area and has actively reached out to other stakeholders in the field of translational immunology and vaccinology.

Impact

Many collaborations among ADITEC supported researchers have been evident during the first year. The work of the ADITEC project is collaborative by nature with 42 partners involved over the 5 year period. During this first year, **12 joint grant applications** were reported as submitted by our partners. **12 joint research projects** were initiated and **four publications were co-authored** between two or more ADITEC partners. The work of 17 of the 19 work packages were designed having partners working across borders, which has promoted and will continue to facilitate extensive collaboration throughout the project. **Three partners** (SigmoidPharma, Emory and SSI) have each joined international initiatives since the start of the project.

External partnerships have been solidified through **three Memoranda of Understanding** executed with TBVI, European Vaccine Initiative and International Aides Vaccine Initiative (IAVI). Representatives from ADITEC meet with high profile funders, regional and national governmental representatives advocating for the importance both from health and economic standpoints.

To date, the ADITEC coordinator has participated in the **submission of one concerted effort** to the European commission. Additional applications are in the planning stages including a Marie Curie fellowship program for training research scientists at all phases of their careers.

One partner has reported leveraged funds from another project, €45.000 from the Euronanomed Research Program.

ADITEC has participated along with the University of Siena and Novartis, in the **creation of Master in Vaccinology and Pharmaceutical Clinical Development**, covering both specific and broad aspects of translational immunology and vaccinology. The training will integrate with existing training schemes and support structures at Partner 39 (NVGH), the ADVAC Course of vaccinology organized by Partner 8 (Unige), the translational vaccinology training at Partner 43 (Surrey), and training modules in adjuvant and vaccine formulation at Partner 22 (WHO). To date, ADITEC sponsored **6 fellowships** for the Masters Programme**, 4 fellowships** in the ADVAC Course and will sponsor up to **12 fellowships** in the coming year These activities coordinate existing courses at a European level, thus promoting knowledge exchange among SME and industrial institutions in participating EU countries.

In just the first year of the five year ADITEC project, impact is being made from new knowledge in the area of vaccines.. The extensive integration of universities, institutes, SMEs and industries built into the ADITEC project will help to close the gap between science and market, and will turn discovery into tangible vaccine products. This knowledge combined with the extensive dissemination plan and synergistic training activities will allow Europe's vaccine sector to keep pace as a leader in one of the quickest growing high tech segments of global business.