FIFTH ANNUAL
NOVEL VACCINES:
Design & Development
August 17-18, 2010

SECOND ANNUAL
PRODUCTION & MANUFACTURING
OF VACCINES
August 17-18, 2010

SECOND ANNUAL
NOVEL VACCINES:
Adjuvants & Delivery Systems
August 18-19, 2010

THIRD ANNUAL
CHALLENGES IN PRE-CLINICAL & CLINICAL DEVELOPMENT
TOP 5 Challenges in Vaccines & Immunotherapies
August 18-19, 2010

Event Highlights:
- 4 Conferences, ONE Location!
- Over 60 Presentations
- Panel Discussions
- Exhibit & Poster Viewing

Pre-Conference Short Courses:
Monday, August 16
Vaccine Business Opportunities: Collaborations, Mergers and Acquisitions
Single-Use Systems (Disposables) for Vaccine Manufacture

Keynotes:
David Cho, Ph.D., M.P.H.
Senior Scientist for Emerging and Pandemic Threat Preparedness, Office of the Director, Center for Biologics Evaluation and Research (CBER), FDA

Norman Baylor, Ph.D.
Director, Office of Vaccines Research and Review (OVRR), Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, FDA

Jay Berzofsky, M.D., Ph.D.
Chief, Vaccine Branch, Center for Cancer Research, National Cancer Institute (NCI), National Institutes of Health

George Siber, M.D.
Director, Selecta Biosciences, and Executive Chairman, Genocea Biosciences

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Collaborations between small and large vaccine developers provide

Melissa Malhame, M.B.A., Senior Director, Dynavax Technologies

4:20 Critical Skills for Effective Alliance Management

will be given.

experienced partners that belong both to academia and the

private sector. It will examine the steps followed for a successful

The past two decades have seen significant progress on

immunization due in part to a favorable policy environment and

partnerships between stakeholders in the public and private sectors. R&D efforts are focused on traditional targets for immunization and also new areas. Vaccines targeted at man-made or emerging natural threats represent development opportunities. Governments and the vaccine industry have invested accordingly. Vaccine development is becoming increasingly more complex but despite this challenge it is anticipated that over the next decade new vaccines will be introduced and the burden of vaccine-preventable infectious diseases will decline.

2:40 Positioning your Product to take Advantage of Business Opportunities in the Vaccine Market

Alan R. Shaw, Ph.D., Chairman, CSO, Vaxinnate Corporation

Taking a vaccine candidate from concept through implementation is a long process with many checkpoints and pitfalls. Questions to consider include the following: is there a public health need for your vaccine and if you make it, will it get used; can you construct a clinical trial that proves it works; can you convince the FDA that it is safe; how do you get the vaccine community on board; how and where will you manufacture your vaccine; do you have a consistent process; do you have a test-release strategy that is robust and informative; what are inspectors most likely to question?

3:15 Refreshment Break

3:45 Experiences of a Recent Collaboration between Private and Public Sectors

Bernd Eisele, M.D., CEO, Vaccine Project Management, GmbH

The talk will report on how we have developed products in a fast and cost-efficient way together with a consortium of well-experienced partners that belong both to academia and the private sector. It will examine the steps followed for a successful collaboration and present a case study. The benefits to both parties will be assessed, and information on handling IP, royalties and terms will be given.

4:20 Critical Skills for Effective Alliance Management

Melissa Malhame, M.B.A., Senior Director, Dynavax Technologies Corp.

Collaborations between small and large vaccine developers provide the potential for utilizing the core competencies and experiences of each player toward a successful product development. Defining “success” and aligning both the scientific and business priorities and levels of risk tolerance for each partner are critical for creating and maintaining successful partnerships. From the perspective of a small player, maximizing the value of collaborations across your portfolio of projects should involve a myriad of approaches, each tailored to the strengths of potential collaborators.

4:55 Discussion

5:30 End of Short Course

Single-Use Systems for Vaccine Manufacture

2:00 Chairperson’s Opening Remarks

Trevor Deeks, Ph.D., Senior Director, Manufacturing Operations and Engineering, Contract Manufacturing Group, Emergent BioSolutions, Inc.

Disposable technologies typically provide flexibility, and reduce capital costs, water utilization, validation time and cost, and equipment footprint. KBI Biopharma has embraced single-use technologies for cell culture based biologics at its multi-product facility. In addition, KBI has developed a proprietary next-generation single-use cell handling technology, kSep®, to fill the gap in the disposable centrifugation area. Challenges and advantages will be discussed.

2:35 Application of Single Use Systems in Dedicated and Multi-Product Vaccine Plants: Implications for Plant Utilization, COGS and Validation

Roman Necina, Ph.D., Site Director Vienna, Intercell, A.G.

At Intercell Biomedical Ltd. Scotland, Intercell’s novel JE vaccine is manufactured in a dedicated plant, whereas at IC USA, the needle-free vaccine patch against Travelers’ Diarrhea (Phase III) and Pandemic Influenza (Phase II) are manufactured in a multi-product plant. In Scotland, single use systems allow best possible utilization of plant capacities for routine, commercial manufacturing. At IC USA, single use systems allow flexible capacity utilization with different products. Application of those systems impacts the design of manufacturing plants as well as the cleaning and process validation approach.

3:05 How Single Use Systems Lend Themselves to Management of Multi-Product Facilities

Howard L. Levine, Ph.D., President, BioProcess Technology Consultants, Inc.

While single-use capsule filters have been used in biomanufacturing for decades, other downstream unit operations, such as chromatography and tangential flow filtration, have been slower to evolve scalable disposable-format technologies. This presentation will provide a review of the driving forces for adoption of single-use technologies as well as an overview of recent advances in disposable-format technologies for downstream processing.

3:35 Refreshment Break

4:00 Implementation of Single-Use Technology in Vaccine Formulation Applications

Donna Riedman, Scientific Services Project Manager, Pall Life Sciences

In this presentation we will address critical applications of single use technology focusing on the challenges, and provide examples including timelines. We will give a brief overview of some key components for formulation & mixing applications, and include validation aspects with especial reference to particulate testing.
4:30 Application of Single Use Systems for Pandemic Preparedness
H. James White, P.E., Executive Director, Engineering & Technical Services, Technical and Quality Operations, Novavax, Inc.
The onset of the H1N1 influenza pandemic brought to light many gaps in global preparedness. The use of single-use systems can reduce the time it takes to build production capacity and get the product to market. This presentation will highlight strategies and benefits related to the use of single-use systems and the potential for use of a regional facility concept in response to a pandemic, as well as challenges in using relatively new technologies in delivering product on a global scale.

5:00 Application of disposable membrane capsules in the manufacture of plasmid DNA for pre-clinical studies
Henry L. Hebel, COO, VGXI Inc.
Two commercially available anion exchange membrane products were compared at process scale regarding DNA binding capacity, contaminant removal and form separation. One had a binding capacity ten-fold that of typical resins. These membrane capsules provide simple, convenient, and economical alternatives to traditional ion exchange chromatography. Their flexibility allows minimized product turn-around time, an essential feature for the manufacture of variable DNA vaccines at large scale for quick response to pandemic threats.

5:30 End of Short Course

*Separate registration required
Tuesday, August 17

7:20am Registration and Morning Coffee

PROTECTING HUMAN HEALTH

8:20 Chairperson’s Opening Remarks

8:30 Opening Keynote Presentation

**FDA’s Approach Towards Pandemic Vaccine Preparedness**

David S. Cho, Ph.D., M.P.H., Senior Scientist for Emerging and Pandemic Threat Preparedness, Office of the Director, Center for Biologics Evaluation and Research (CBER), FDA

When the 2009 H1N1 influenza virus emerged in the spring of 2009, the Food and Drug Administration (FDA) worked with our sister agencies within the Department of Health and Human Services (HHS), other U.S. government agencies, the World Health Organization (WHO), foreign governments, sister regulatory agencies, and vaccine manufacturers to facilitate the development, production, and availability of safe and effective vaccines against the 2009 H1N1 virus. This combined effort allowed for vaccines to be made, licensed, and delivered to people in record time. This presentation will highlight FDAs approach towards pandemic vaccine preparedness and the regulatory challenges that the 2009 H1N1 vaccine presented.

9:15 Influenza Virus-Like Particle Vaccine Produced in Insect Cells Elicits Hemagglutination and Neuraminidase Inhibiting Antibodies in Immunized Healthy Adults

Steven Pincus, Ph.D., Executive Director, Analytical Operations, Novavax, Inc.

Historically, influenza vaccines have been standardized by their hemagglutinin content and influenza immunity has been measured by determining the level of hemagglutinin inhibiting antibody. To meet the need for improved vaccine with an enhanced immunogenic profile in the elderly, we have developed a technology to produce influenza virus like particles (VLPs) engineered to co-express the HA, NA and M1 proteins. A trivalent vaccine was produced for the 2008-2009 vaccine strains (A/Brisbane/59/2007 H1N1, A/Brisbane/10/2007 H3N2, B/Florida/4/2006). When administered to healthy adults in a Phase II study at 15µg and 60 µg doses, the vaccine was well tolerated and elicited 57-86% 4-fold rise post immunization in HAI titers and 50-73% 4-fold rise post immunization in NAI titers. The VLPs can be used to measure HA immunological responses in a similar manner to live flu virus.

9:45 New Pneumococcal Vaccines: Protein, Conjugate and Hybrid Vaccine Strategies

Mark Alderson, Ph.D., M.B.A., Director, Pneumococcal Vaccine Project, PATH

The goal of PATH’s pneumococcal vaccine project is to accelerate the development of promising new pneumococcal vaccines that are safe and effective in young children, and to ensure their affordability, availability, and use in developing countries. As part of this project, PATH is developing a portfolio of potential vaccine candidates with a particular emphasis on “common protein” vaccines. Vaccines containing proteins that are common to all pneumococcal serotypes could provide broad and affordable protection to children worldwide. Our current protein vaccine partnerships range from novel methods of antigen discovery to well characterized vaccine candidates that have provided protection in multiple animal models and are currently in early stages of clinical evaluation. A second strategy involves the development of a killed, whole cell vaccine, also designed to offer broad serotype-independent coverage coupled with low manufacturing costs and ease of administration.

10:15 Networking Coffee Break with Exhibit and Poster Viewing

HIV

11:00 Challenges to Develop an HIV Vaccine – The Need for Multiple Approaches

Thomas Hassell, Ph.D., VP, Vaccine Development, International AIDS Vaccine Initiative

Epidemiological figures published by UNAIDS in 2009 confirm a stark reality; the number of people living with HIV in 2008 reached 33.4 million, with 7,400 new infections per day. An AIDS vaccine is believed to be the best hope of ending the pandemic and IAVI (The International Aids Vaccine Initiative) is dedicated to this purpose. With our partners, we hope to capitalize on a number of recent and exciting scientific advances to overcome the enormous challenges inherent in AIDS vaccine development. Progress with these multiple approaches will be presented at the conference.

11:30 Development of an HIV Vaccine: Challenges and Successes

Indresh Srivastava, Ph.D., Associate Director, Vaccines Research, Protein Biochemistry, Novartis Vaccines & Diagnostics, Inc.

The focus of the HIV project at Novartis is to design and develop a novel Envelope (Env) based HIV vaccine that is able to induce cross-neutralizing antibody responses against diverse primary isolates. We are evaluating several complimentary approaches to enhance the exposure of conserved functional epitopes to improve the ability of Env for inducing potent neutralizing antibodies with special emphasis on two approaches: a) to target conserved functional epitopes involved in co-receptor binding for eliciting cross reactive neutralizing antibody responses; b) evaluate Env derived from the early primary isolates that may have better exposure of the critical epitopes involved in virus binding and entry compared to the late isolates, which may be better suited for vaccine development.

12:00pm How to Overcome Cold Chain Challenges

Tim Redmond, Director, Regional Accounts, World Courier, Inc.

In the ever-expanding market of Cold Chain Management, the challenges presented become more complex. In this presentation we will focus on the key factors involved in successful Cold Chain Management. These key factors are, but are not limited to, Planning & Communication, Temperature Profiling, Chain of Custody, Packaging, Temperature Monitoring & Reporting, SOP and Excursions. We will share our experiences and knowledge to offer a practical guide for success in this complex arena.

12:15 FlugEM™, a New Intranasal Vaccine to Prevent Influenza

Govert J. Schouten, Chief Executive Officer, Mucosis B.V.

Mucosis’s lead program FlugEM™ is aimed at developing a new influenza vaccine that can be administered to humans by a simple
radiation-attenuated PfSPZ. Such PfSPZ could be non-replicating (as attenuated PfSPZ that are not only more potent, but also as safe as techniques can be used to create a parasite clone that will produce manufacture. We are also determining whether genetic targeting the next clinical trial. In parallel efforts are underway to optimize the radiation-attenuated parasite vaccine has been shown to induce lasting sterile protection in humans and in animal models. Here we discuss the development of genetically attenuated parasites (GAPs) as the next generation platform to produce a safe and reproducible, whole-cell malaria vaccine that prevents infection at the pre-erythrocytic stage. Current clinical development of the first generation of GAP vaccines will also be presented.

Development of a Metabolically Active Non-Replicating Sporozoite Vaccine to Prevent Malaria Caused By Plasmodium Falciparum

Peter Billingsley, Ph.D., Senior Director, Entomology and Quality Systems, Sanaria

An ideal vaccine for malaria would target all stages of the parasite life cycle, and thereby prevent infection, severe disease and transmission. However, most malariologists agree that if only one stage is to be targeted, it should be the pre-erythrocytic stage, because induction of highly protective immune responses against this stage will prevent blood stage infection and thus disease, and parasite transmission. Our consortium is working to develop such a vaccine. The first-generation vaccine is a metabolically active, non-replicating Plasmodium falciparum sporozoite (PfSPZ) vaccine that is attenuated by irradiation. The first major challenge was to manufacture adequate quantities of such a vaccine that met regulatory standards for initial clinical trials, and demonstrate it was safe, well tolerated and immunogenic in humans. This has been accomplished. The second major challenge is to determine how to administer for the first time in humans an unprecedented, non-replicating and metabolically active (live) whole-organism vaccine formulation composed of PfSPZ that measure 0.5–1.0 µm x 7–10 µm so as to induce > 85% protection. Volunteers immunized by intradermal (ID) or subcutaneous (SC) routes were protected in the first clinical trial. However the number of protected subjects was low, and despite a dose response, immunogenicity was sub-optimal. Animal studies show that intravenous (IV) immunization induces much better immunity and protection than immunization by the SC or ID routes. These data have been used to inform the design of the next clinical trial. In parallel efforts are underway to optimize non-IV administration of PfSPZ, and the efficiency and scale-up of manufacture. We are also determining whether genetic targeting techniques can be used to create a parasite clone that will produce attenuated PfSPZ that are not only more potent, but also as safe as radiation-attenuated PfSPZ. Such PfSPZ could be non-replicating (as are radiation-attenuated PfSPZ), replication deficient, or replication competent, but avirulent. Our goal is to develop, license and deploy a highly effective pre-erythrocytic stage PfSPZ vaccine that prevents blood stage infection, disease, and transmission. Such a vaccine could be used at the community level in Pf elimination campaigns, and at the individual level for prevention of Pf malaria in infants, young children, and pregnant women in endemic areas, as well as individuals of all ages who travel to malaria-endemic areas.

The development of dengue vaccines has been ongoing for decades and has proven to be very challenging. A key concern is the perceived need for a balanced tetravalent response in order to minimize the risk of vaccine-induced exacerbated disease. Traditional methods for vaccine development (e.g. live-attenuated viruses) showed early promise with products advancing to Phase 2 clinical development. However, manufacturing issues and the inability to achieve balanced, properly attenuated formulations led to delays or outright termination. Hawaii Biotech, Inc. (HBI) is pursuing the development of a recombinant subunit protein vaccine comprised of antigens that maintain native-like structure. This approach offers potential advantages over live attenuated and chimeric approaches in terms of safety, dosing regimen, and ease of adjusting the tetravalent balance. Progress for the various dengue vaccine development programs will be presented and the challenges remaining for the field discussed.

TB Vaccine Development

Lewellys F. Barker, M.D., M.P.H., Senior Medical Advisor, Aeras Global TB Vaccine Foundation

Much progress in TB vaccine research and development over the past decade has been accomplished through partnerships between the public, private, and academic sectors via nonprofit organizations like the Aeras Global TB Vaccine Foundation. The main focus is on developing a heterologous prime-boost vaccine regimen that could include a replacement for current BCGs such as a recombinant BCG as the prime, and boosting with one of several novel vaccine candidates, including viral vectored and fusion protein vaccines. A number of vaccine candidates are in clinical trials in the US, Europe and Africa, and several other candidates are in the pipeline. The goals for a new TB vaccine regimen are safety, including in people infected with HIV, and increased efficacy against TB disease.

Immunotherapy for Prostate Cancer: Explaining the Conundrum of Improved Survival without Improvement in Time to Progression

Ravi A. Madan, M.D., Assistant Clinical Investigator, Lab of Tumor Immunology & Biology, The Center for Cancer Research (CCR), National Cancer Institute (NCI), NIH

Recent clinical data in prostate cancer suggest significantly improved overall survival without any improvement in time to progression. I will present data from recent clinical trials suggesting that both the kinetics of an anti-tumor immune response and impact of an anti-tumor immune response on subsequent therapies may explain this. I will also explain how these concepts may impact which patient populations should be enrolled in immunotherapy clinical trials and provide data from randomized studies. There is considerable confusion within the medical oncology community about how to interpret the overall survival data for immunotherapy studies and what can explain improvements in overall survival. The
Because the presence of even small amounts of naturally occurring antibody to the thrombomodulin-friedreich cancer antigen TF-Ag is related to improved prognosis, our target Ag is TF-Ag. Our goal is to develop a vaccine that will result in an immune response to TF-Ag in the patient in order to improve prognosis. Several approaches (peptide mimics, constructs with B cell epitopes attached to immune enhancing agents) are being developed. An immune response to TF-Ag could improve the prognosis in breast, colon, bladder, prostate and other carcinomas, thus this vaccine has great clinical potential. Strategies to improve the immune response to carbohydrate antigens also have potential to impact bacterial and viral vaccines.

**5:15 Carbohydrate Tumor Antigen Vaccines Using Unique Strategies**
Kate Rittenhouse-Olson, Ph.D., Professor, Director, Biotechnology Program, Biotechnical and Clinical Laboratory Sciences, The University at Buffalo

Using the Bordetella pertussis protein pertactin as a model, we have applied synthetic scaffolds in order to mimic structurally defined epitopes by confined presentation of several different peptide arms. In addition, dendrimers are employed in multivalency approaches. Using the Bordetella pertussis protein pertactin as a model, we have shown that protective antibodies can be obtained directed towards a discontinuous epitope. However, the structural ability of linear peptides to achieve an adequate mimicry of the structure of a protein is limited. Therefore, we have developed efficient approaches for the preparation of peptide-loops, which provide better mimics of the native shape of a protein having loops, turns, etc. Moreover, the exploration of efficient and convenient approaches is pursued for attachment of these peptide-loops to synthetic scaffolds as well as to dendrimers and polymers for multivalency. These approaches may open up new avenues towards mimicry of protein surfaces and protein discontinuous epitopes towards fully synthetic vaccines.

**9:00 Filamentous Phage as a Carrier for Conjugate Vaccines**
Jamie Scott, Ph.D., Professor, Molecular Biology & Biochemistry, Simon Fraser University

The surface of the filamentous bacteriophage comprises ~2600 primary amine-reactive sites for conjugation spaced ~37 angstroms apart. As such, phage can be used as highly immunogenic carriers for peptides and haptenes that have been chemically conjugated to its surface. We have engineered the phage to remove immunodominant epitopes on its surface, so as to enhance the antibody response against weakly immunogenic peptides or carbohydrates. This approach succeeded in improving the antibody response against a peptide, and we are currently attaching short carbohydrate chains to the phage coat to mimic the “glycan shield” of the HIV-1 envelope, with the goal of eliciting HIV-1-neutralizing antibodies. I will report our progress in this project, along with an investigation of the anti-phage B-cell response that should provide a means for controlling and improving antibody response against targeted molecules.

**9:30 “Universal” Influenza Vaccine: Progress and Challenges**
Hersh Mehta, Ph.D., Head, Product Conception and Development, sanofi pasteur Biologics

Unlike current vaccines that are based on hemagglutinin (HA) protein, which varies structurally between different type A influenza strains and also seasonally within subtypes, vaccine development based on conserved M protein has recently gained considerable interest. If successful, this approach can address challenges associated with seasonal influenza vaccines and/or pandemic preparedness. We have used a region of M protein that is significantly conserved between type A influenza viruses, genetically fused with carrier protein, and expressed the chimeric protein in E.coli. The product self assembles into well defined structures of 30nm virus-like particles that are composed of protein and RNA. Accelerated stability studies provided understanding of probable mechanism of degradation for improving formulation during life cycle management. Following acceptable toxicological studies, clinical trial in humans showed safe and immunogenic responses. Challenges in product development will be discussed.
vaccine. We have successfully developed an Ad5 [E1-, E2b-] against Carcinoembryonic Antigen (CEA) to treat colon cancer patient. I will present pre-clinical, process development, manufacturing and early clinical data on the use of Ad5 [E1-, E2b-]-CEA vaccine.

11:45 Novel Platform for Low Cost, Orally Administered Vaccines: Replication Competent Adenovirus Vectored Vaccines Produced In A549 Human Lung Cells

Deborah A. Mosca, Ph.D., Vice President, Project Management, PaxVax Inc.

PaxVax has developed a proprietary replicating vaccine vector technology that can express protein antigens from bacteria, viruses, or parasites. To date, using these methods, more than 80 Adenovirus serotypes 4 and 7 vectored products have been designed, produced and tested for functional expression of the transgene products and/or immunogenicity. These include recombinant Ad4 vectors encoding hemagglutinin from multiple strains of influenza (e.g. H5N1, H1N1, and seasonal variants), protective antigen from anthrax, and envelope proteins from HIV.

In order to achieve low cost productivity for our novel Ad4 vectored vaccines, we compared replication of our vectors in a number of cell substrates derived from various human organs such as lung (MRC-5, A549, H1299), colon (CaCo2, SW480), duodenum (HuTu 80), liver (HepG2), and cervix (HeLa). The results demonstrated that A549 was far superior for production of Ad 4 than other cell substrates. In addition, A549 meets the criteria for an optimal cell substrate such as tropism for the cell, productivity per infected cell, cell density, and the ability to adapt to serum free and suspension culture. PaxVax has prepared a Master Cell Bank (MCB) of adherent A549 cells and is in the process of completing release tests in concordance with the FDA guidance. Vials from a Working Cell Bank (WCB) will be made available to others interested in evaluating the suitability of A549 for other applications.

The potential advantages of PaxVax orally administered, replicating Ad4 vector vaccines compared to traditional injectable vaccines for recipients include convenience, ease of administration, lower dosage and potential for enhanced immunogenicity with a replicating vector, and lower delivery costs. The advantages of such vaccines for society at large include faster manufacturing, ease of stockpiling and more rapid distribution to the needy.

12:15pm End of “Novel Vaccines: Design & Development” meeting
Tuesday, August 17

7:20am  Registration and Morning Coffee

REGULATORY UPDATE / CELL LINES AND PRODUCTION PLATFORMS

8:20  Chairperson’s Opening Remarks
Michael Dekleva, Ph.D., Senior Director, Worldwide Regulatory Affairs, Merck Sharp & Dohme Corporation

8:30  OPENING KEYNOTE PRESENTATION
Regulatory Authority Perspective on Handling Vaccine Production, Manufacturing and Process Change
Norman Baylor, Ph.D., Director, Office of Vaccines Research and Review, Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, FDA
This talk will address industry concerns regarding the importance of validation of the manufacturing process and validation of assays and will examine assessment of the immunological response. It will offer practical advice on managing manufacturing change and putting together a comparability package, and provide examples of changes that have required approval including incidents of when clinical data have been required.

9:15  Production of Influenza Vaccines Using a Fungal Production Platform
Debbie Higgins, VP, Vaccine Development, Neugenesis Corporation
New technologies for producing influenza vaccines are needed. A Neurospora crassa fungal production platform is being developed to rapidly produce large amounts of immunogenic and protective influenza virus-like particles (VLPs) containing hemagglutinin, neuraminidase and matrix 1 protein. Host cell growth is extremely fast, the system is completely animal-free, and virus growth is not required. Production strains can be stably stored and the system can be used to generate tailored multivalent vaccines.

9:45  Case Study on Designer Duck Cell Lines and Vectored Vaccines AGE1-CR: A Production Platform for Vectored Vaccines
Volker Sandig, Ph.D., VP, Probiogen, A.G.
Modern vaccines require efficient scalable production processes. Permanent cell lines growing to high cell densities overcome limitations associated with primary cells and chicken eggs and are endorsed by industry. With a defined history and well characterized cell banks they provide a better documentation and higher safety margin and enable the development of virus and protein products with unique properties. The cell line AGE1.CR was created by directed immortalization of retina cells of a single Muscovy Duck embryo and extensively tested following EMEA and FDA guidelines. They represent the core of a versatile vaccine and protein production platform. We will discuss challenges and solutions for scaling production of pox- and alphavirus-vectored vaccines.

10:15  Networking Coffee Break with Exhibit and Poster Viewing

PROCESS DEVELOPMENT, OPTIMIZATION, AND VALIDATION

11:00  Optimization of a Process for an Attenuated Influenza Vaccine Produced on Vero Cells
Thomas Muster, Ph.D., CEO, AVIR Green Hills Biotechnology, A.G.
Avir Green Hills Biotechnology is developing a cell culture-based production system for a replication-deficient live attenuated influenza vaccine. The vaccine is produced on Vero cells and a chromatography based purification process is being successfully employed for the pilot-scale production for clinical phase 1 and 2 material. A case-study addressing challenges such as strain-change variations, process optimization, and scale-up to commercial scale manufacturing will be presented.

11:30  Designing and Validating a Manufacturing Process
Trevor Deeks, Ph.D., Senior Director, Manufacturing Operations and Engineering, Contract Manufacturing Group, Emergent BioSolutions, Inc.
This presentation links the Quality by Design (QbD) concept with the validation activities required for the process. It looks at the early stages of process design at a very high level through the technique of process mapping to identify the key inputs and outputs from the process, how they need to be studied to provide an understanding of the process, the importance of establishing process robustness and the need to characterize the process. The presentation will cover the validation and other documentation aspects briefly and will also provide some advice on establishing the validation requirements and realistic acceptance criteria. Finally it will look at things that go wrong and how they may be avoided.

12:00pm  Luncheon Presentation

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FOCUS ON DOWNSTREAM PROCESSING & MAINTAINING STERILITY

1:55  Chairperson’s Remarks
Tony Brazzale, BIA Separations, Inc.
2:00 Challenges and Solutions to Downstream Bioprocessing Operations for the Manufacture of Vaccine Candidates

Timothy Lee, Ph.D., Deputy Director, Bulk Manufacturing, sanofi pasteur

A systematic methodology for the clarification of bacterial proteins for extracellular or intracellular bacterial proteins is described. The chosen methodology was based on process economics, recovery and purity of the clarified material prior to downstream column purification. We selected centrifugation for the initial step of clarification. For extracellular proteins, a final ultrafiltration step is usually performed, and for intracellularly-expressed proteins, clarification using microfiltration and final ultrafiltration is preferred. Other methods such as a direct capture step and ion-exchange membrane technologies were also investigated to determine if they could reduce downstream steps, improve recovery and reduce overall process cost while maintaining high purity.

2:30 Purification Development for a Live Attenuated Influenza Virus from MDCK Cell Culture

Simon Hsu, Ph.D., Principal Scientist, Vaccine Process Biochemistry, MedImmune, Inc.

The increasing demand for seasonal flu vaccine and risk of a pandemic pose an unprecedented challenge to current egg-based manufacturing. MedImmune has developed a MDCK cell culture production platform. Cellufine® Sulfate (CS) affinity gel column chromatography was used to purify the influenza virus. This was a key step for degraded host cell DNA (HCD) removal in the presence of Benzonase®. For scale-up from 20L cell culture to 400L, the capacity of CS gel was further explored. HCD levels in this second generation process were reduced and helped to increase the CS column dynamic binding capacity by more than three fold.

3:00 Discussion and Networking

3:30 Networking Refreshment Break with Exhibit and Poster Viewing

STABILITY AND FORMULATION, AND COLLABORATION FOR MANUFACTURING OUTSIDE THE US AND EU

4:15 Spray Drying in Vaccine Manufacturing for Improved Stability

Tom Jin, M.D., Scientist, Principal Investigator, Technique Operations & Manufacturing, Aeras Global TB Vaccine Foundation

Based on our AERAS 402 vaccine, the benefits and challenges of manufacturing spray dried products will be discussed. Shorter processing cycle time and larger batch size per unit operation compared with lyophilization improve the commercial application of the spray drying technique. However, challenges exist in transferring the concept into a final product, such as: 1) Developing a stable formulation that gives a high recovery during the spray drying process and is hydrophobic during shelf storage; 2) The aseptic cGMP spray dryer design; 3) Powder filling; 4) Developing economic unit-dose packs or blister capsules for final product and DPI; 5) Cost effectiveness.

4:45 Development of a Recombinant Vaccine to Treat Vaginal Candidiasis – From the Bench to Clinical Testing

Christian Spyr, Ph.D., Head, Project Management and Clinical Development, Pevion Biotech, Ltd.

Vaginal Candida infections have emerged as a significant medical problem during the last few decades. Innovative vaccine approaches are needed to induce local mucosal immunity in order to cure recurrent vulvovaginal candidiasis. In animal challenge studies, recombinant Secreted Aspartyl Proteinases-antigen (Sap2) delivered by influenza virosomes are able to induce protective immune responses. An innovation vaccine delivery system (Influenza virosomes, VLP) combined with a new application form will be presented. In addition, the tech transfer from lab scale to cGMP production scale will be discussed. The vaccine candidate is currently in a phase 1 clinical study.

5:15 Scale-Up of a Plasmid DNA Purification Process Based on PlasmidSelect Xtra for Production of GMP Grade pDNA For Vaccination and Transfection Clinical Studies

Tony Hitchcock, Head, Manufacturing Technologies, RecipharmCobra Biologic Ltd.

This presentation will be based around work performed within RecipharmCobra Bio, using the Plasmid Select Xtra resin to improve and enhance an existing production platform used for the large scale production of clinical grade plasmids. It will focus on works performed with challenging plasmids with inherently high levels of host DNA and open plasmid circle forms, and subsequent works performed to streamline the process, to reduce processing times and operational costs.

5:45 Reception with Exhibit and Poster Viewing

6:45 End of Day

Wednesday, August 18

7:30am Morning Coffee (Breakfast Sponsored Presentation Opportunity Available)

SCALE-UP AND RAPID RESPONSE TO PANDEMICS

8:25 Chairperson’s Remarks

Mark W. Thompson, R.Ph., Ph.D., Director, Vaccine Process Biochemistry, Vaccine Development, MedImmune, Inc.

8:30 Scale-Up of an Intensified Process for rAd35 Adenovirus Production using the PER.C6® Cell Substrate

Herman van Herk, M.Sc., Scientist, Up-Stream Process Development, Crucell Holland B.V.

Our recombinant tuberculosis adenovirus based vaccine (rAd35) is currently in several Phase I trials with promising results, and in a recently started Phase II study. Given the uncertainties required to develop a 10,000-liter facility and the need to develop a 10,000L scale viral vaccine manufacturing process, we are focusing on intensification of rAd35 manufacturing using the PER.C6® cell substrate. We will show a 10-fold intensification at bench scale and, for the first time, results of the scaled-up upstream process in 50L single-use bioreactors and the impact on cost of goods at production scale.

9:00 Technical Challenges and Solutions for Development, Manufacturing Scale-Up and Management of Seasonal Strain Changes for Recombinant Influenza Vaccine

Albert Price, Ph.D., Technical Director, Influenza, Protein Sciences Corporation

FluBlok® (Protein Sciences Corporation) is a recombinant cell-based trivalent influenza vaccine produced using the baculovirus expression system. The product is currently under regulatory review by the FDA. An important challenge in the development of FluBlok was the implementation of a robust, cost-effective manufacturing process with the flexibility to respond quickly to annual influenza vaccine changes. This case-study will examine solutions to unique challenges encountered in manufacturing different influenza hemagglutinins, including: managing strain-change variations at key steps of upstream and downstream processing, key points for process optimization, and challenges anticipated for commercial scale manufacturing. Strategies for further improvement will also be discussed.

9:30 Staying Live: Scale-Up of an Attenuated Respiratory Syncytial Virus (RSV) Vaccine

Mark W. Thompson, R.Ph., Ph.D., Director, Vaccine Process Biochemistry, Vaccine Development, MedImmune, Inc.

Respiratory Syncytial Virus (RSV) is an important respiratory pathogen of infants and young children, causing annual epidemics of bronchiolitis and pneumonia worldwide. Severe RSV illness
commonly occurs among infants with primary infection in the first year of life and RSV is estimated to cause as much as 90% of all childhood bronchiolitis and up to 40% of all paediatric pneumonias. MedImmune is developing a cell culture-based production system for the RSV vaccine. A case study discussing the optimization of the manufacturing process, and challenges faced during development and scale-up strategies will be presented.

**10:00 Networking Coffee Break with Exhibit and Poster Viewing**

**WORKING WITH THE REGULATORY AUTHORITIES / PRODUCT QUALITY AND ANALYTICAL CHARACTERIZATION**

**10:45 After the License Approval - What Can Analytics Do?**

*C. Brent Oswald, Ph.D. Associate Director, VMSC–Bioanalytics, Merck Manufacturing Division*

Getting a BLA approved for a new vaccine can be a daunting task, but keeping the market supplied after licensure of a successful vaccine can be an even bigger challenge. Analytics can play an important role in keeping product supplied to the marketplace, especially during the critical launch phase. The talk will describe the application of analytical comparability to GARDASIL®, Merck’s novel new vaccine to prevent cervical cancer, in order to bridge product produced by a launch facility to that produced by a scale-up facility without the need for a clinical trial. This effort assured a smooth transition of supply and fulfilled marketing needs during the critical catch-up market phase for this product. Analytical tools are also important to sustain the market for older vaccine products which have been licensed for decades. In this case, the issues involved in modernization of the release methods will be discussed. Of particular note will be the special issues for bridging potency assay procedures for legacy products.

**11:15 Industry Perspective on Handling the Complex and Sometimes Undefined Regulatory Requirements**

*Michael Dekleva, Ph.D., Senior Director, Worldwide Regulatory Affairs, Merck Sharp & Dohme Corporation*

Past and recent experiences with vaccines have reinforced their medical and commercial significance, and the uniqueness of the process development and life cycle management challenges that they present to manufacturers. CBER and international regulatory authorities exist in a state of dynamic tension between their missions to rapidly introduce new products to satisfy unmet medical needs, and ensure patient safety. Manufacturers are likewise driven to expedite new vaccine introductions, and must satisfy expectations for vaccine quality, safety, and efficacy through well-orchestrated strategies for product development and global registration. Manufacturers must also establish and maintain a robust manufacturing, quality, and regulatory infrastructure to ensure an uninterrupted supply after launch. This presentation will provide practical insights into the strategic challenges associated with vaccine development and life cycle management.

**11:45 Meeting Regulatory Challenges through Better Characterization of Vaccine Production Substrates**


Recent scientific and technological advances have created new opportunities to develop vaccines and introduce new vaccine production substrates. In spite of a large body of research data generated over the years, characterization of these new production substrates, especially those related to their use in vaccine production, is still lacking. This has led to concerns and additional uncertainties during regulatory review and product approval. We shall discuss a novel approach that helps us to address some of these issues and to assess tumorgenicity and oncogenicity of mammalian cells *in vitro*.

**12:15pm End of “Production & Manufacturing of Vaccines” meeting**
Responses

Cytokines and Toll-Like Receptor Ligands as Adjuvants to Improve the Quality as well as Quantity of T Cell Immune Responses

Jay A. Berzofsky, M.D., Ph.D., Chief, Vaccine Branch, Center for Cancer Research, National Cancer Institute (NCI), National Institutes of Health

We have examined cytokines and synergistic combinations of toll-like receptor agonists as defined molecular adjuvants to improve not only the quantity, but perhaps more importantly, the quality of the T cell immune response to vaccines. In particular, we find that IL-15 as an adjuvant can select for higher avidity CD8+ T cells that are more effective at clearing virus infections and tumors, and can also substitute for CD4+ T cell help to induce long-lived memory CD8+ T cell responses. We have also found two double combinations of TLR ligands that can synergistically increase the magnitude of CD8+ T cell response as measured by tetramer staining, as well as increase the activation of dendritic cells. However, only a triple combination of TLR ligands was sufficient to induce strong protection against a vaccinia virus challenge of mice, and this protection depended not on a further increase in T cell numbers, but rather an increase in their functional avidity.

Modulating Vaccine Responses with Innate Immunity

Bali Pulendran, Ph.D., Professor, Pathology, Emory University School of Medicine

Despite their great success, we understand little about how effective vaccines stimulate protective immune responses. Two recent developments promise to yield such understanding: the appreciation of the crucial role of the innate immune system in sensing microorganisms and tuning immune responses, and advances in systems biology. In this presentation, I will discuss how these developments are yielding insights into the mechanism of some of the most successful vaccines ever developed. Furthermore, such developments promise to address a major challenge in vaccinology: that the efficacy of a vaccine can only be ascertained retrospectively, upon infection. The identification of molecular signatures induced rapidly after vaccination, which correlate with and predict the later development of protective immune responses, would represent a strategy to prospectively determine vaccine efficacy. Such a strategy would be particularly useful when evaluating the efficacy or immunogenicity of untested vaccines, or in identifying individuals with sub-optimal responses amongst high risk populations, such as infants or the elderly. We have recently used a systems biology approach to identify early gene signatures that correlate with, and predict the later immune responses in humans vaccinated with the live attenuated yellow fever vaccine YF-17D, or with the influenza vaccines. I will review these studies, and discuss their broader implications for vaccinology.

TLR3 Adjuvants Improve Oral Gene-Based Immunization

Sean Tucker, Ph.D., Founder, VP Research & CSO, Vaxart, Inc.

Oral gene-based vaccination has several potential advantages over current injected vaccines. Among these advantages are the ability to quickly distribute vaccines to areas of the world where medical care is inadequate or disrupted, to permit rapid transition from antigen gene to product through well-characterized manufacturing methods, and potentially, to avoid the problems of pre-existing immunity to the vector. The problem is that oral vector vaccination has generally performed poorly in larger animal models. Vaxart has developed an expressed TLR3 adjuvant that has substantially improved the oral vaccine performance, making oral immunization better than an injected vaccine and protective against diseases such as influenza and Venezuelan Equine Encephalitis. Unlike an injected vector, the immune responses generated are substantially selective against the antigen of choice, making this a platform, not a single use technology.

ENHANCING THE IMMUNE RESPONSE

Toll-Like Receptor 4: The Use of MPL in Vaccines – Efficacy and Safety Evaluation

Nathalie Garçon, Ph.D., VP & Head, Research & N. American R&D, GlaxoSmithKline Biologicals

Improved understanding of the important role of TLR signalling in the induction of adaptive immune responses has led to the discovery of TLR agonists. A strong immunostimulant and a specific TLR4 agonist guiding the immune system towards a Th1 response is lipopolysaccharide (LPS). 3-O-desacyl-4’-monophosphoryl lipid A (MPL), a derivative of LPS, is to date the best characterised TLR4 agonist, and is part of the adjuvant combination AS04, an Adjuvant System consisting of MPL adsorbed onto a particulate form of aluminium salt. As LPS, MPL acts via TLR4 pathway, resulting in a transient and localised enhanced production of cytokines and chemokines leading to the maturation and migration of APCs to the draining lymph nodes. This results in improved adaptive immune responses as evidenced by increased antibody titres and memory cells. Preclinical data show that MPL has no direct impact on effector T and B cells. AS04 is currently used in licensed vaccines for HBV (FENDrix™) and HPV (Cervarix®). An AS04-containing candidate vaccine, for HSV, is currently in phase III clinical trials. AS04 has consistently demonstrated its ability to induce a high neutralising antibody response. Both the HPV vaccine and HSV candidate vaccine elicited increased antibody levels at the site of infection via transudation from the serum to the mucosa. The HPV and HBV vaccines induced more durable protective antibody levels, thus decreasing the number of vaccine doses required. In clinical studies, AS04-formulated HPV and HBV vaccines have been shown to have acceptable reactogenicity and safety profiles comparable to classic aluminium adjuvanted vaccines.

Enhancement of Response to Vaccines with the Use of an Immune Modulating Peptide, Thymosin Alpha 1

Israel Rios, M.D., CMO & Senior VP, SciClone Pharmaceuticals, Inc.
5:45 Vaccine Adjuvants and Regulatory Considerations
William M. Egan, Ph.D., Vice President, PharmaNet Consulting
Live-attenuated viral and bacterial vaccines (including vectored vaccines), as well as many older generation vaccines (such as the various killed, whole-cell vaccines), were “self-adjuvanted,” incorporating molecular motifs that are recognized by, and activate, the innate immune system. Many newer vaccines, such as those based on recombinant proteins, will require vaccine adjuvants and, moreover, will often require non-aluminum salt based adjuvants. The development of appropriate adjuvants for particular vaccines, both from efficacy as well as safety viewpoints, will, ideally, be based on the known mechanisms of action of the potential adjuvants; these considerations may, as well, be influenced by the intended vaccine recipient population, for example, neonates or the elderly. Regulatory decisions, either to allow a clinical trial to proceed or, eventually, to license a product, will be based on perceived or demonstrated risks and benefits associated with the particular vaccine and its associated adjuvant. This presentation will discuss a number of factors (such as, adjuvant manufacture and characterization, pre-clinical studies supporting efficacy and safety, risk-minimization strategies, and eventual Phase 4 studies) that may be incorporated into such risk-benefit algorithms.

5:15 Vaccine Immune-Enhancing Delivery Systems: From Danger Signals to a Nutritive Approach in Vaccine and Adjuvant Design
Michael Vajdy, Ph.D., CEO, EpitoGenesis, Inc.
Since the dawn of ancient and modern vaccination strategies the focus of vaccine developers has been to activate danger signals in the host cells in order to mimic the pathogen. While this approach has yielded several effective vaccines which in some cases have eliminated the disease altogether, in some other cases it has proven toxic. Indeed, as recently as two years ago a live attenuated based HIV vaccine was proven to be unsafe. Also recently, a mutant toxin-based adjuvant also proved to be unsafe in Phase I Clinical trials. In this talk I will give an overview of various popular vaccine adjuvant and delivery systems, leading to our own approach in this area: Given the crucial issue of vaccine safety we opted for an approach in vaccine design in which we addressed the safety issue first. Thus, we selected components of a nutritive vaccine immune enhancing delivery system (NIDS) based on their proven safety in humans as edible nutrients. We have now tested the NIDS mixed with antigens from viral and bacterial pathogens in animal studies and demonstrated higher antibody and CD4-derived cytokine responses compared to vaccinations without NIDS. Our studies demonstrate that this approach is effective and by definition safe and may lead to a new era in vaccine and adjuvant design.

6:15 End of Day

Thursday, August 19

7:30am Morning Coffee (Breakfast Sponsored Presentation Opportunity Available)

DNA VACCINES

8:25 Chairperson’s Remarks

8:30 Heterologous Prime-Boost Vaccines for HIV Vaccine Development
Shan Lu, M.D., Ph.D., Professor, Medicine, University of Massachusetts Medical School
Development of an HIV vaccine faces some unusual challenges. Two traditional vaccine modalities, the live-attenuated and inactivated vaccines, are considered either too risky or insufficient to elicit strong and broad B and T cell immune responses against a virus with diverse and constant genetic mutations. The failure of a subunit-based protein vaccine further denied HIV vaccine researchers the privilege of using this previously successful vaccination approach. The surprising failure of the “STEP trial,” which focused solely on T cell immune responses, a dramatic shift from the traditional reliance on antibodies for vaccine development, finally closed the door for an attempt towards developing an HIV vaccine based on a single vaccination approach. Our finding that a polyvalent DNA prime-protein boost vaccine can elicit balanced and broadly cross-reactive antibody and T cell immune responses including positive neutralizing antibodies in humans indicated that a combination vaccination approach provides an alternative strategy to allow for the elicitation of complicated protective immune response required for an HIV vaccine.

9:00 Designing Smarter Adenoviral Vector Delivery of Vaccines: What Has Translated Successfully into Humans
Alfredo Nicosia, Ph.D., CSO, Okairos
Okairos develops genetic vaccines for major infectious diseases, including malaria, hepatitis C (HCV) and universal influenza, using a novel proprietary technology. Okairos’ technology platform is based on the development of new, potent, replication-incompetent Adenovirus vectors, derived from strains isolated from chimpanzees and used to encode and deliver prophylactic and therapeutic antigens. These vectors are not neutralized by human sera, and they hold promise for generating effective T cell responses, where existing vectors have failed. Development of these new Adenovirus vectors from preclinical- to clinical stage will be presented along with the generation of an optimised cell substrate for their production.

9:30 SynCon DNA Vaccines for Emerging Infectious Diseases
Niranjan Y. Sardesai, Ph.D., Senior VP, Research & Development, Inovio Pharmaceuticals
The 2009 outbreak of the newly emergent swine origin influenza A/H1N1 and its rapid escalation to a pandemic designation by the WHO, has drawn attention to the need to develop vaccine approaches that are broadly protective against related yet divergent virus strains. DNA vaccines afford many advantages desirable for a rapid response to an emerging pandemic – easy to produce within weeks, store, transport, and deploy; and are considered safer than live virus vaccines. Similarly, current strain-matched influenza vaccine approaches place a severe limitation on their use against emergent strains and results in the need for new vaccines every year. We will discuss the development of Syncon™ DNA vaccine candidates based on consensus antigens to target multiple unmatched but related pandemic and seasonal influenza strains and demonstrate broadly cross-protective immune responses in
animal models of disease. The same strategy has been extended to target other emerging infectious diseases such as dengue and chikungunya that also require broadly cross-protective immune responses.

10:00 Networking Coffee Break

MODES OF DELIVERY

10:30 The Pharmajet Needle-Free System for Standard Delivery of H1N1 Flu Vaccines and Future Applications Enabled by Intra-Dermal Delivery
Linda McAllister, M.D., Ph.D., Chief Medical Officer & VP, R&D, PharmaJet, Inc.
PharmaJet’s low cost and robust needleless jet injection system is now FDA, CE and ANVISA cleared for intramuscular and subcutaneous delivery. The initial commercial experience of patients and healthcare workers with H1N1 and seasonal flu vaccinations will be presented. In addition, Intra-dermal delivery can reduce vaccine dose and adjuvant requirements; the future use of this new modality will be discussed.

11:00 Mucosal Immunization against Vaginal Candida Infections Using Sap2 Recombinant Protein Delivered by Influenza Virosomes
Rinaldo Zurbriggen, Ph.D., Senior Program Manager, Biopharma Manufacturing, Lonza AG
Vaginal Candida infections have emerged as a significant medical problem during the last few decades. Innovative vaccine approaches are needed to induce local mucosal immunity in order to cure recurrent vulvovaginal candidiasis. In animal challenge studies, recombinant Secreted Aspartyl Proteinases-antigen (Sap2) delivered by influenza virosomes are able to induce protective immune responses. A Phase I clinical study is ongoing.

11:30 Intranasal Nanoemulsion Adjuvanted Influenza Vaccine – Dose Range Efficacy and Toxicity Studies
Tarek Hamouda, M.D., Ph.D., M.B.A., Director of Vaccines, NanoBio Corporation
NB-1008 is a nanoemulsion adjuvanted Fluzone® vaccine. The adjuvant is an oil-in-water emulsion composed of nanometer-sized droplets stabilized by surfactants. Different doses of commercial influenza vaccine (Fluzone®) were mixed with different concentrations of nanoemulsion and administered intranasally to ferrets to determine immune responses. IND-enabling rabbit toxicity studies were performed under GLP conditions. The ferret and rabbit studies demonstrated that administration of NB-1008 resulted in an unprecedented high titer of antibody response without toxic side effects. These studies led to initiation of a first-in-man clinical trial in 2009.

12:00pm Sponsored Presentation (Opportunity Available)

12:15 Mimopath™, A New Versatile Vaccine Carrier-Adjuvant Technology
Kees Leenhouts, Chief Scientific Officer, Mucosis B.V.
Mucosis’s vaccine technology Mimopath™ is based on bacteria-like particles derived from the food-grade bacterium Lactococcus lactis. The particles can simply be used as an adjuvant or can also be functionalized as antigen carrier. Mimopath™ has been shown to activate the innate immune system through TLR2. Vaccines based on Mimopath™ raise balanced Th1/Th2 type responses that are protective as demonstrated in several models for viral, bacterial and parasitic diseases. The Mimopath™-based vaccines are suitable for mucosal and parental routes of administration.

PARTICULATE DELIVERY

1:45 Chairperson’s Remarks

1:50 How VLPs Develop Their Efficacy
Mario Amacker, Ph.D., Head, Process Development & Manufacturing, Pevion Biotech, Ltd.
Virome are a clinically and commercially validated VLP technology. They are used for several marketed and currently developed subunit vaccines. Despite their use in licensed vaccines, little is known about how they act. We present how this carrier/adjuvant system generates its effect and how this will affect the future development of subunit vaccines. We are able to describe a clear mode of action that may be applicable to other VLPs. This is the first time that a novel adjuvant/carrier system is described in such detail. This information is key for future regulatory approval processes, not only for the virome VLP but for VLPs in general.

2:20 Synthetic Virus-Like Particle (SVLP) Technology in Synthetic Vaccine Design
Arin Ghasparian, Ph.D., CSO, Virometix AG
A new approach to vaccine delivery has been developed that is based on artificial nanoscale biological assemblies in the 20–30 nm size range. The assemblies resemble small viruses and VLPs in their shape and composition (i.e. they contain lipid and protein), and harness their excellent immunostimulatory properties, but are made entirely by chemical synthesis. Antigens of choice, including drug-like hapten, small synthetic proteins and synthetic antigen mimetics (SAMs), can be coupled to these “Synthetic Virus-like particles” (SVLPs) for multivalent presentation in an ordered repetitive format. The properties of SVLPs can be tailored using a myriad of chemical methods to include pathogen associated molecular patterns, such as toll-like receptor ligands, as well as a universal T-helper epitopes and pathogen-specific T-cell and B-cell epitopes. The talk will illustrate the SVLP approach with artificially designed SVLPs that combine B-cell epitope mimetics and a universal T-helper epitope from the malaria parasite P. falciparum that are strongly immunogenic in animal models without use of an adjuvant.

2:50 Lecithin Nanoparticles as an Adjuvant for Vaccines
Zhengrong Cui, Ph.D., Associate Professor, College of Pharmacy, The University of Texas at Austin
An accumulation of research over the years has demonstrated the utility of nanoparticles as antigen carriers with adjuvant activity. We engineered novel nanoparticles from lecithin/glycerol monostearate-in-water emulsions. Using bovine serum albumin (BSA), ovalbumin (OVA), or Bacillus anthracis protective antigen (PA) protein as model antigens, we defined the adjuvanticity of the nanoparticles when the antigens were covalently conjugated onto their surface and evaluated the effect of the size of the nanoparticles on the resultant immune responses. The potent adjuvant activity of the nanoparticles was likely due to their ability to move the antigens into local draining lymph nodes, to enhance the uptake of the antigens by antigen-presenting cells, and to activate the antigen-presenting cells. This novel nanoparticle system has the potential to serve as a universal protein-based vaccine carrier capable of inducing strong immune responses.

3:35 Adjuvantage of a Vaccine without Adjuvant Injection
Mei Y. Wu, M.D., Ph.D., Associate Professor, Wellman Center for Photomedicines, MGH/Harvard Medical School
We develop a laser-based vaccine “adjuvant” capable of enhancing and prolonging immune responses against both model and clinical vaccines, with few side effects locally or systemically. Brief illumination (2 min) of a small area (< 0.7 cm2) of the skin with a non-destructive safe laser boosted the production of ovalbumin
(OVA)-specific antibody by 300~500% over intradermal OVA injection. Similarly, the level of flu-specific antibody was 9-folds higher after two vaccinations with a season flu vaccine each following laser illumination as compared to the vaccine alone. Moreover, immunization of monophosphoryl lipid A (MPL)-adjuvanted OVA followed by laser illumination of the administration site increased the amount of OVA-specific antibody from 11-folds with MPL to 22-folds with MPL plus laser illumination. Thus, in comparison with all current vaccine adjuvants that are either chemical compounds or biological agents, laser-based adjuvant platform is a potent, long-term risk-free vaccine “adjuvant” as it can adjuvantate a vaccine without injection of any self or foreign substance into one’s body.

4:05  Clinical Safety of the ISCOMATRIX Adjuvant
Marli Watt, M.D., Clinical Safety Physician, Clinical Safety, CSL Limited

ISCOMATRIX™ adjuvant is a novel saponin based adjuvant which can be administered with various antigens to induce a targeted immune response. It is a component of a number of vaccines undergoing clinical investigation. The challenge is to manage an integrated approach to patient safety across a diverse range of programs, and evaluate the adjuvant-specific risk benefit profile. The development program for a novel vaccine adjuvant has many distinctive features compared to that of conventional products in clinical development, which include the associated unique challenges faced in managing a range of evolving safety data in order to analyze an adjuvants’ clinical risk – benefit profile. This is particularly pertinent in our current climate, with new technologies, ever increasing scrutiny over vaccine constituents, and evolving expectations from both Regulators and the Public regarding potential undesirable side effects. This presentation will address these challenges and describe CSL’s proactive approach to evaluating and managing the safety profile of our novel adjuvant.

4:35  End of ImVacS
A greater understanding of the complex responses to experimental immunotherapeutics will facilitate the identification of biomarkers that predict clinical outcome. We have developed a broad-based immunomonitoring platform based on 14-color multiparametric flow cytometry for high resolution analysis of induced immune responses to our RNA-loaded DC immunotherapy. Interim conclusions from clinical immunomonitoring data using this method and techniques for analyzing these large data sets will be discussed.

ANALYZING POST-MARKETING SURVEILLANCE AND EPIDEMIOLOGY

5:15 Cohort Event Monitoring – A Description of Methodology and Tools
Magnus Wallberg, M.Sc., Head, Systems Development Strategies, Production, Development and Quality, the Uppsala Monitoring Centre

The growing use of vaccines in public health programs in both developed and developing countries has increased the need to identify any safety issues as soon as possible – so that actions can be taken. The WHO and the Uppsala Monitoring Centre (UMC) have proposed a methodology called Cohort Event Monitoring that can be used to monitor safety in vaccination programs and also developed CemFlow which is a web-based tool that is perfectly suited to gather relevant information in a format that is optimized for analysis and signal detection. Use of CemFlow will add ‘real life’ information to the limited data obtained in clinical trials and give insight in the profile of events that occur following administration of the vaccine(s) in the population that was monitored. The presentation will give insight in the potential benefits of Cohort Event Monitoring and a brief introduction to CemFlow.

5:45 End of Day
HSPC-96 in patients with recurrent GBM (multi-center) and newly diagnosed GBM (single-center). HSPC-96 vaccine therapy is well-tolerated with no serious adverse events attributable to vaccine. An interim review of patients with recurrent GBM (Phase 1/2 trial; n=32), demonstrated a median survival of 44 weeks post-resection. Further, all patients exhibited innate and adaptive immune response. In newly diagnosed GBM (n=8; trial-initiated 2009), there have been no toxicities associated with concurrent treatment of HSPC-96 and temozolomide. Clinical and immunologic evaluation is ongoing.

9:30  Cancer Vaccine Forum Immunotherapies & Adjuvants

What are some of the challenges for testing immunotherapies, specifically for cancer, in the presence of adjuvants? Panelists will identify and address these challenges, in addition to answering audience questions and comments.

Moderator: Bruce L. Levine, Ph.D., Director Director, Clinical Cell & Vaccine Production Facility, Research Associate Professor, Pathology and Laboratory Medicine, University of Pennsylvania

Panelists:
- Michael Kalos, Ph.D., Director, Translational and Correlative Studies Laboratory, University of Pennsylvania School of Medicine
- James Gulley, M.D., Ph.D., Director, Clinical Trials Group, Laboratory of Tumor Immunology and Biology, The Center for Cancer Research (CCR), National Cancer Institute, NIH
- Andrew T. Parsa, M.D., Ph.D., Associate Professor in Residence of Neurological Surgery, Principal Investigator, Brain Tumor Research Center, University of California, San Francisco
- Robert Hawkins, Ph.D., Professor, Medical Oncology, University of Manchester, Coordinator, ATTACK Project

10:00  Networking Coffee Break

10:25  Chairperson’s Remarks

Bruce L. Levine, Ph.D., Director, Clinical Cell & Vaccine Production Facility, University of Pennsylvania

10:30  Strategies for the Non-Clinical Safety Assessment of Vaccines

Jayanthi Wolf, Ph.D., Associate Director, Safety Assessment, Merck & Co., Inc.

This presentation will provide considerations for developing non-clinical safety assessment programs for vaccines. Regulatory guidelines from the EMEA, WHO, and U.S. FDA will be outlined, which address the non-clinical safety assessment of vaccines. The choice of a relevant animal model, types of toxicology studies, design of the treatment schedule, and the ante-mortem and post-mortem parameters investigated will be described.

11:00  Evaluation of the Safety and Efficacy of a Novel RSV F Particle Vaccine in the Cotton Rat

Ramadevi Raghunandan, Ph.D., Senior Scientist, Immunology, Novavax

Novavax evaluated a novel RSV F particle vaccine in cotton rat pre-clinical studies and found it to be immunogenic and efficacious without any evidence of disease enhancement following RSV challenge. Immunization of cotton rats with the RSV F particle vaccine plus aluminum phosphate adjuvant resulted in high titers of neutralizing antibody against RSV with no enhanced disease pathology at any doses as measured by lung histopathology and absence of plaque forming virus in lung homogenates of cotton rats exposed to RSV. In contrast, the formalin inactivated RSV vaccinated group did not produce neutralizing antibody, had very high lung histopathology scores and significant plaque formation in the lungs. Cotton rats serve as excellent model for RSV induced pulmonary disease since they are susceptible to RSV infection and in this study, highlighted the contrast between the enhanced disease associated with formalin inactivated RSV and the safety and efficacy profile demonstrated by the RSV F particle vaccine.

11:30  Engineering T-cells for Cancer Therapy

Robert Hawkins, Ph.D., Professor, Medical Oncology, University of Manchester, Coordinator, ATTACK Project

Presentation covers aspects of pre-clinical and clinical development of engineered T-cell therapy. The issues of adequacy of pre-clinical models to assess toxicity will be discussed. Also included are the challenges of producing patient specific therapy.

12:00pm  Sponsored Presentation (Opportunity Available)

12:15  Luncheon Presentation (Opportunity Available) or Lunch on Your Own

1:50  Developing a Potency Assay for the Variable Component of the Autologous, Protein Based Therapeutic Cancer Vaccine, Oncophage

Daniel L. Levey, Ph.D., Senior Director Scientific Affairs, Antigenics Inc.

It is an inconvenient truth that potency of fully autologous cancer vaccines derives from the individually tumor specific antigens present in each patient’s tumor. For a cancer vaccine like Oncophage, assessing such antigens’ contribution to potency on a lot by lot basis is outside the realm of technical possibilities without likely depleting the entire supply of each patient’s product. Antigenics’ approach to this challenge will be discussed.

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Navigating the Regulatory Minefield with a Novel Cell Substrate

Daniel Adams, President & CEO, Protein Sciences

Protein Sciences’ expresSF+® cell line derived from insect ovary cells was developed in the early 1990s and has been used to make products that have been in more than 20 clinical trials involving both human and veterinary therapeutic and prophylactic vaccines. One veterinary vaccine is marketed worldwide and several human vaccines are in clinical trials including two that are late stage (FluBlok®, our recombinant subunit influenza vaccine that we expect to receive marketing approval for this year) and Diamyd®, a customer’s Type I diabetes vaccine that is in Phase III in the U.S. and E.U. The presentation will discuss the trials and tribulations of securing FDA sign off on a novel insect cell line.

4:35  End of ImVacS Conference
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**Pre-Conference Short Courses**

- **Monday, August 16 • 2:00-5:00 PM**
- **SC1: Single-Use Systems (Disposables) for Vaccine Manufacture**
- **SC2: Vaccines Business Opportunities: Collaborations, Mergers & Acquisitions**

**Poster Discount**

- **$50 off**
- **$50 off**

**Register 3 - 4th Is Free**

Individuals must register for the same conference or conference combination and submit completed registration form together for discount to apply. Please reproduce this registration form as needed.

**Group Discounts Available!** Special rates are available for multiple attendees from the same organization.

- **For more information on group discounts contact David Cunningham at 781-972-5472**

**Payment Information**

- **Enclosed is a check or money order payable to Cambridge Healthtech Institute, drawn on a U.S. bank, in U.S. currency.**
- **I invoice me, but reserve my space with credit card information listed below.**
- **Invoices unpaid two weeks prior to the conference will be billed to your credit card at the full registration rate. Invoices must be paid in full and checks received by the deadline date to retain the registration discount.**
- **All attendees of CHI’s events will receive a complimentary subscription of CHI’s Molecular Med Monthly e-newsletter.**

**Substitution/Cancellation Policy**

In the event that you need to cancel a registration, you may:

- **Transfer your registration to a colleague within your organization.**
- **Credit your registration to another Cambridge Healthtech Institute program.**
- **Request a refund minus a $100 processing fee per conference.**
- **Request a refund minus the cost ($350) of order if you may:**

**Handicapped Equal Access**

In accordance with the ADA, Cambridge Healthtech Institute is pleased to arrange special accommodations for attendees with special needs. All requests for such assistance must be submitted in writing to CHI at least 30 days prior to the start of the meeting.

**Registration to: Cambridge Healthtech Institute**

250 First Avenue, Suite 200, Needham, MA 02444

T: 781-972-5400 F: 781-972-5425

www.healthtech.com

CHI Insight Pharma Reports

- A series of diverse reports designed to keep life science professionals informed of the salient trends in pharmaceutical technology, business, clinical development, and therapeutic disease markets.
- For a detailed list of reports, visit InsightPharmaReports.com or contact Rose LaRia, rlaria@healthtech.com, 781-972-5444.

Barnett Educational Services

- Barnett is a recognized leader in clinical education, training, and reference guides for life science professionals involved in the drug development process. For more information, visit www.barnettinternational.com.

**Additional Registration Details**

Each registration includes all conference sessions, posters and exhibits, food functions, and access to the conference proceedings link.

**Group Discounts**

- Special rates are available for multiple attendees from the same organization. Contact David Cunningham at 781-972-5472 to discuss your options and take advantage of the savings.

- **Handicapped Equal Access**

- **Substitution/Cancellation Policy**

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